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USPC 552/510; 514/177
See application file for complete search history.

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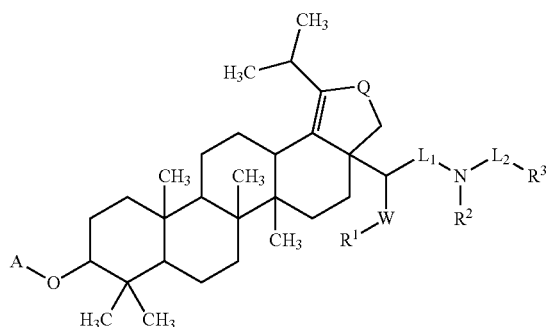
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(57) **ABSTRACT**

The present invention relates to compounds characterized by having a structure according to the following Formula I:



or a pharmaceutically acceptable salt thereof. Compounds of the present invention are useful for the treatment or prevention of HIV.

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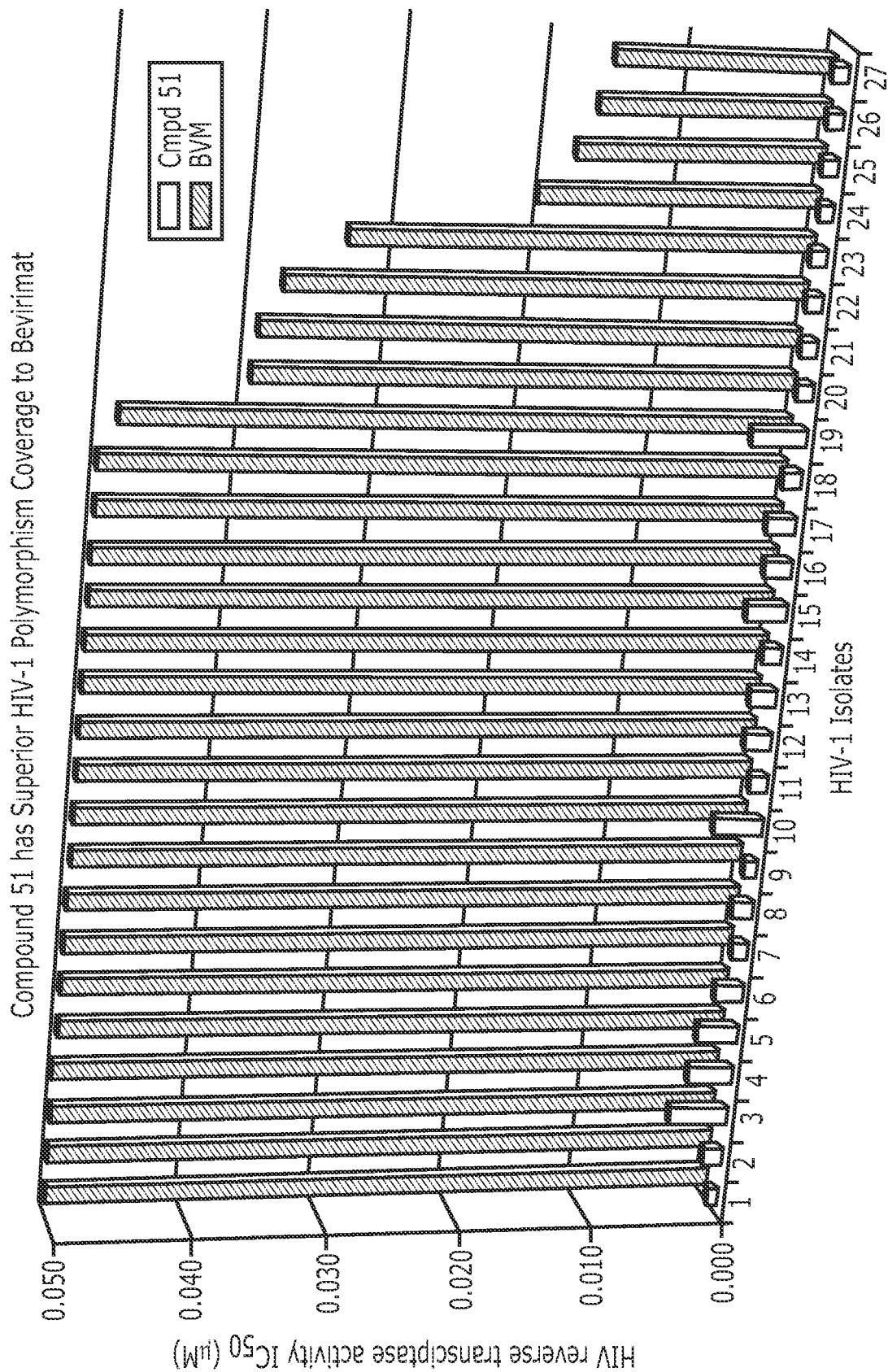


Figure 1

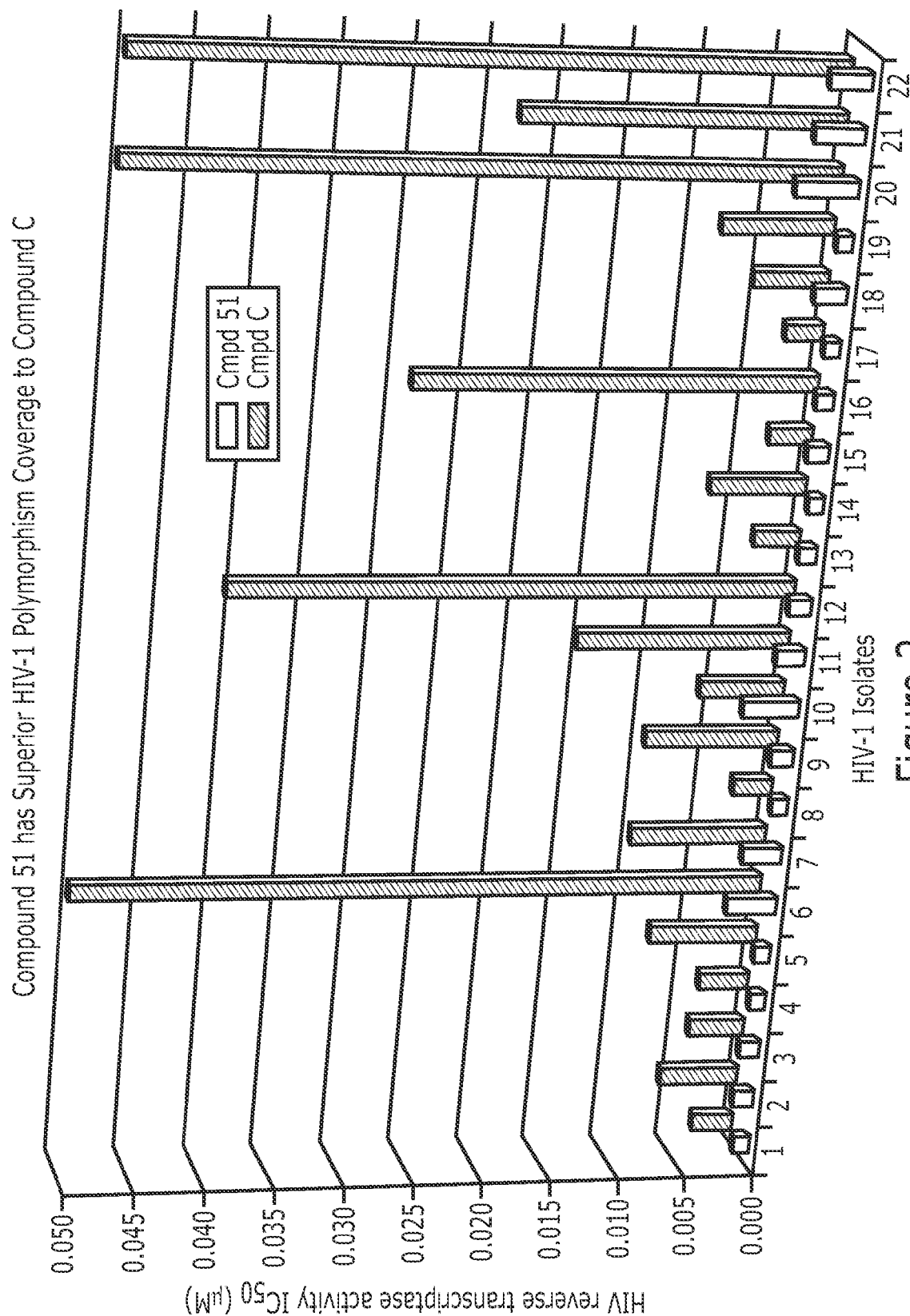


Figure 2

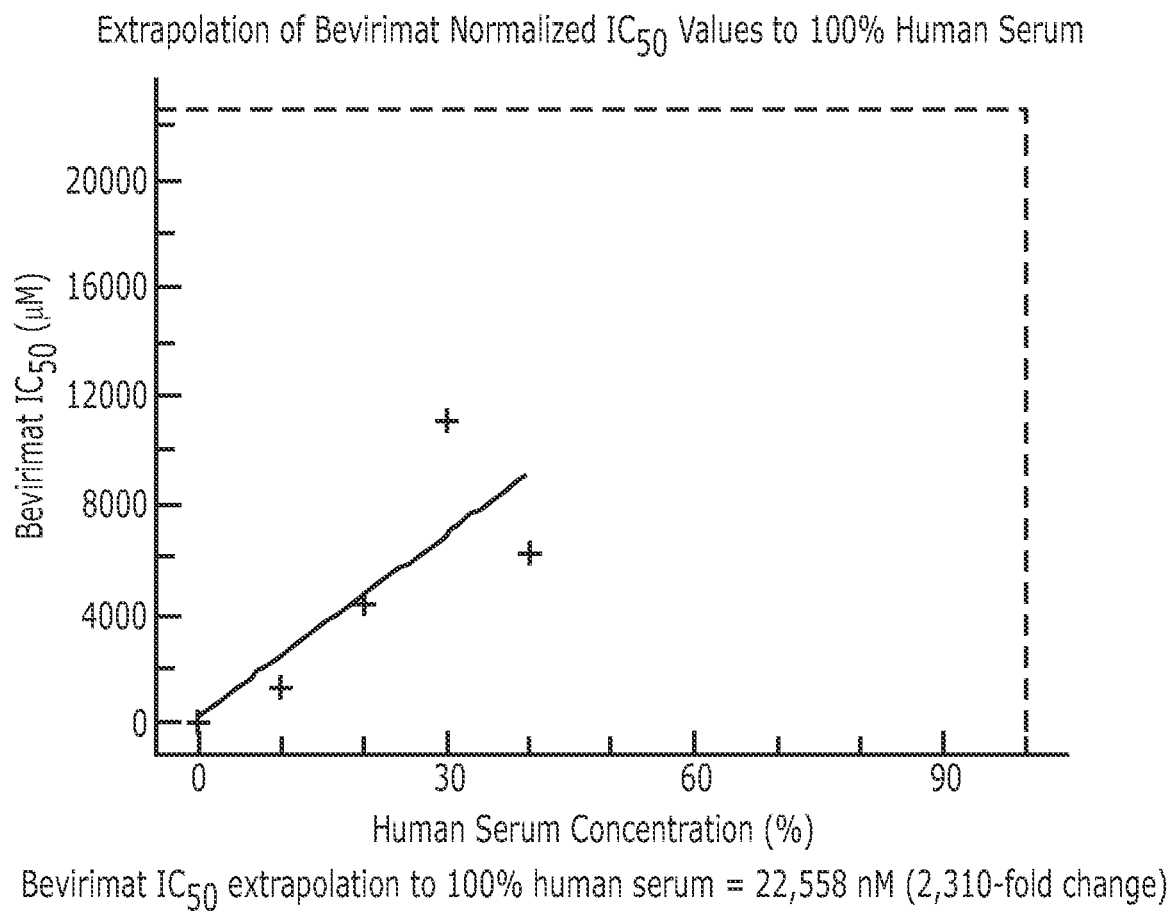
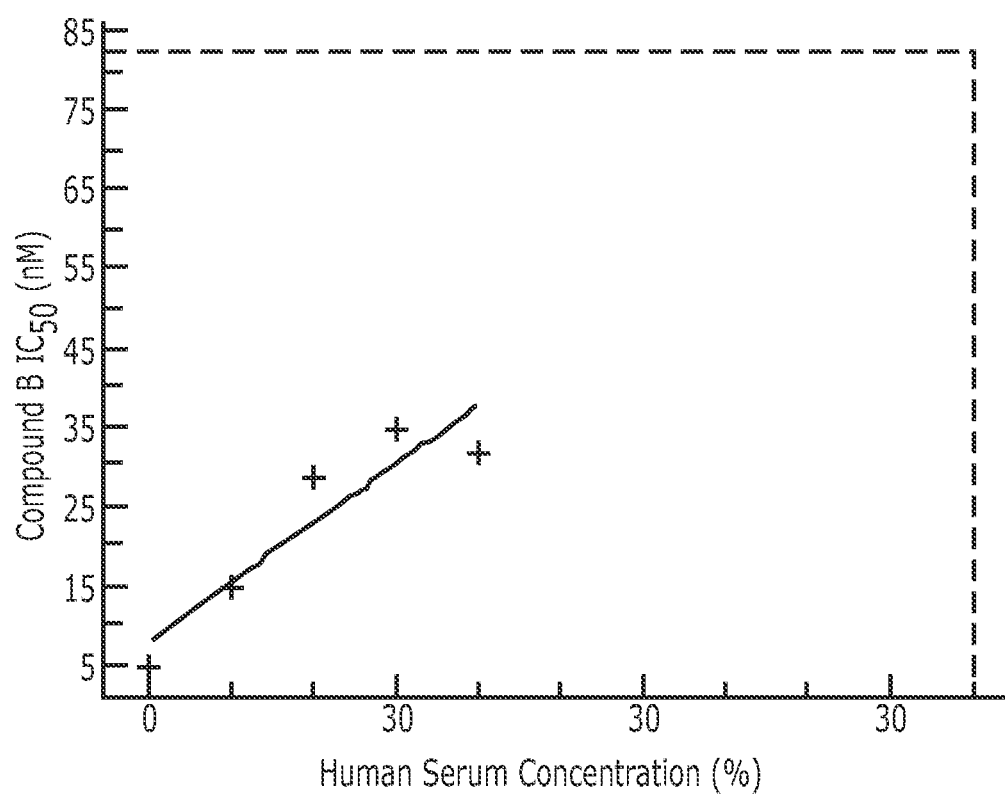


Figure 3

Extrapolation of Compound B Normalized IC_{50} Values to 100% Human Serum



Compound B IC_{50} extrapolation to 100% human serum = 82.0 nM (17-fold change)

Figure 4

Extrapolation of Compound 51 Normalized IC_{50} Values to 100% Human Serum

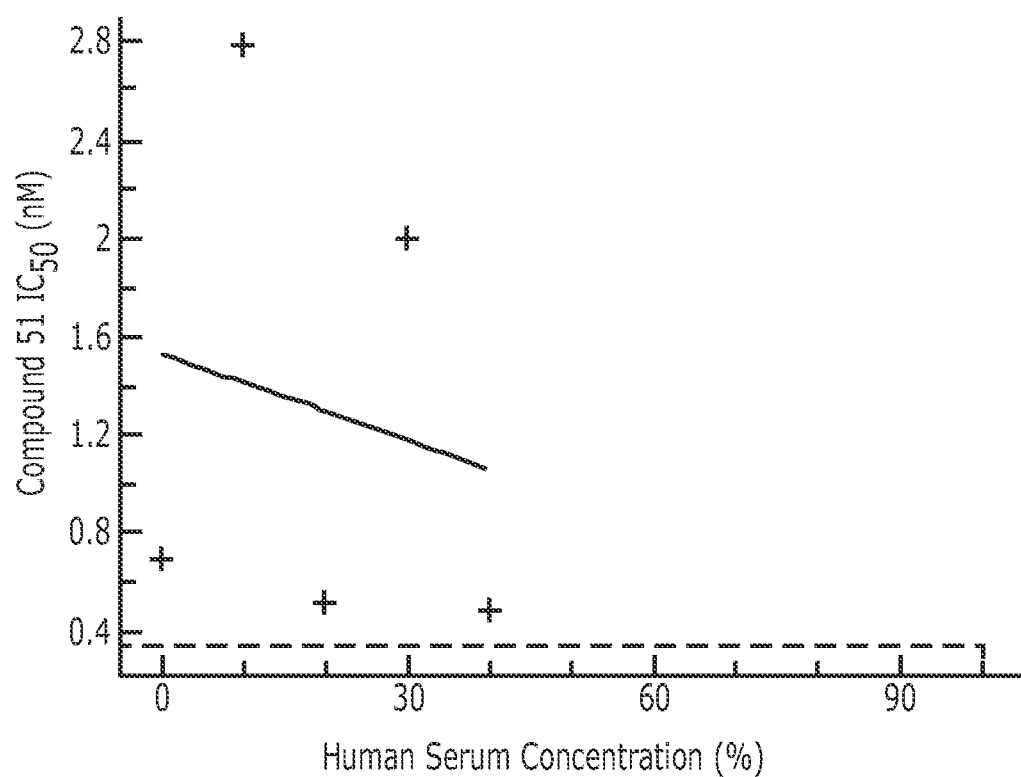


Figure 5

DERIVATIVES OF BETULIN**CROSS REFERENCE TO RELATED PATENTS
AND PATENT APPLICATIONS**

This is a U.S. Non-provisional Patent Application and claims the benefit of U.S. Provisional Patent Application No. 61/576,448, filed on Dec. 16, 2011, which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

The present invention relates to compounds, pharmaceutical compositions, and methods of use thereof for (i) inhibiting HIV replication in a subject infected with HIV, or (ii) treating a subject infected with HIV, by administering such compounds.

BACKGROUND OF THE INVENTION

Human immunodeficiency virus type 1 (HIV-1) leads to the contraction of acquired immune deficiency disease (AIDS). The number of cases of HIV continues to rise, and currently over twenty-five million individuals worldwide suffer from the virus. Presently, long-term suppression of viral replication with antiretroviral drugs is the only option for treating HIV-1 infection. Indeed, the U.S. Food and Drug Administration has approved twenty-five drugs over six different inhibitor classes, which have been shown to greatly increase patient survival and quality of life. However, additional therapies are still required because of undesirable drug-drug interactions; drug-food interactions; non-adherence to therapy; and drug resistance due to mutation of the enzyme target.

Currently, almost all HIV positive patients are treated with therapeutic regimens of antiretroviral drug combinations termed, highly active antiretroviral therapy ("HAART"). However, HAART therapies are often complex because a combination of different drugs must be administered often daily to the patient to avoid the rapid emergence of drug-resistant HIV-1 variants. Despite the positive impact of HAART on patient survival, drug resistance can still occur. The emergence of multidrug-resistant HIV-1 isolates has serious clinical consequences and must be suppressed with a new drug regimen, known as salvage therapy.

Current guidelines recommend that salvage therapy includes at least two, and preferably three, fully active drugs. Typically, first-line therapies combine three to four drugs targeting the viral enzymes reverse transcriptase and protease. One option for salvage therapy is to administer different combinations of drugs from the same mechanistic class that remain active against the resistant isolates. However, the options for this approach are often limited, as resistant mutations frequently confer broad cross-resistance to different drugs in the same class. Alternative therapeutic strategies have recently become available with the development of fusion, entry, and integrase inhibitors. However, resistance to all three new drug classes has already been reported both in the lab and in patients. Sustained successful treatment of HIV-1-infected patients with antiretroviral drugs will therefore require the continued development of new and improved drugs with new targets and mechanisms of action.

Presently, long-term suppression of viral replication with antiretroviral drugs is the only option for treating HIV-1 infection. To date, a number of approved drugs have been shown to greatly increase patient survival. However, therapeutic regimens known as highly active antiretroviral therapy (HAART) are often complex because a combination of different drugs must be administered to the patient to avoid the rapid emergence of drug-resistant HIV-1 variants. Despite the positive impact of HAART on patient survival, drug resistance can still occur.

The HIV Gag polyprotein precursor (Pr55Gag), which is composed of four protein domains—matrix (MA), capsid (CA), nucleocapsid (NC) and p6—and two spacer peptides, SP1 and SP2, represents a new therapeutic target. Although the cleavage of the Gag polyprotein plays a central role in the progression of infectious virus particle production, to date, no antiretroviral drug has been approved for this mechanism.

In most cell types, assembly occurs at the plasma membrane, and the MA domain of Gag mediates membrane binding. Assembly is completed by budding of the immature particle from the cell. Concomitant with particle release, the virally encoded PR cleaves Gag into the four mature protein domains, MA, CA, NC and p6, and the two spacer peptides, SP1 and SP2. Gag-Pol is also cleaved by PR, liberating the viral enzymes PR, RT and IN. Gag proteolytic processing induces a morphological rearrangement within the particle, known as maturation. Maturation converts the immature, donut-shaped particle to the mature virion, which contains a condensed conical core composed of a CA shell surrounding the viral RNA genome in a complex with NC and the viral enzymes RT and IN. Maturation prepares the virus for infection of a new cell and is absolutely essential for particle infectivity.

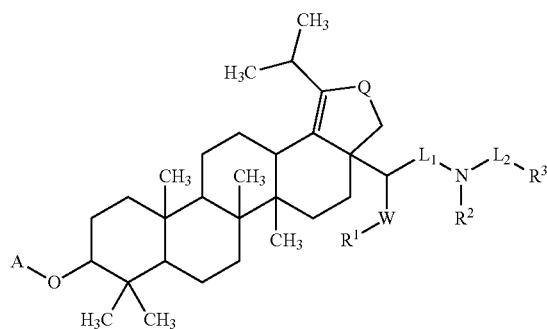
Bevirimat (PA-457) is a maturation inhibitor that inhibits the final step in the processing of Gag, the conversion of capsid-SP1 (p25) to capsid, which is required for the formation of infectious viral particles. Bevirimat has activity against ART-resistant and wild-type HIV, and has shown synergy with antiretrovirals from all classes. Bevirimat reduced HIV viral load by a mean of 1.3 log₁₀/mL in patients who achieved trough levels of ≥ 20 μ g/mL and who did not have any of the key baseline Gag polymorphisms at Q369, V370 or T371. However, Bevirimat users with Gag polymorphisms at Q369, V370 or T371 demonstrated significantly lower load reductions than patients without Gag polymorphisms at these sites.

Other examples of maturation inhibitors can be found in PCT Patent Application No. WO2011/100308, "Derivatives of Betulin"; PCT Patent Application No. PCT/US2012/024288, "Novel Anti-HIV Compounds and Methods of Use Thereof"; Chinese PCT Application No. PCT/CN2011/001302, "Carbonyl Derivatives of Betulin"; Chinese PCT Application No. PCT/CN2011/001303, "Methylene Derivatives of Betulin"; Chinese PCT Application Nos. PCT/CN2011/002105 and PCT/CN2011/002159, "Propenoate Derivatives of Betulin". Maturation inhibitors in the prior art leave open gaps in the areas of polymorphism coverage whereby potency against a broad range of clinically relevant gag sequences is extremely important, along with overall potency including the clinically relevant protein adjusted antiviral activity that will be required for robust efficacy in long term durability trials. To date, no maturation inhibitor has achieved an optimal balance of these properties.

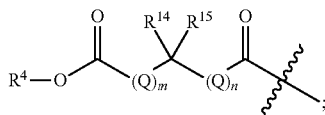
It would therefore be an advance in the art to discover alternative compounds that are an effective balance of the aforementioned properties for the prevention and/or treatment of HIV infections.

SUMMARY OF THE INVENTION

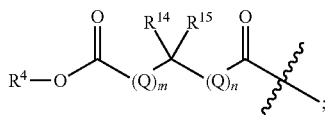
In accordance with one embodiment of the present invention, there is provided a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein:
A is

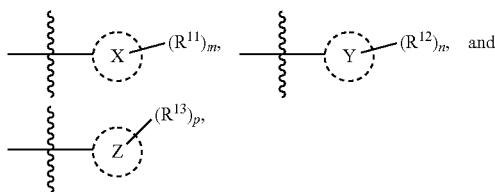


L₁ and L₂ are independently selected from a bond or [C(R⁶)]_q;
each instance of Q is independently selected from —CH₂— or —C(=O)—;
W is selected from a bond or O;
R¹ is selected from the group consisting of hydrogen, (C₁-C₁₂)alkyl, —C(O)R⁵, —CH₂—O—(C₁-C₆)alkyl, 2-tetrahydro-2H-pyran, and



R² is selected from the group consisting of —H, (C₁-C₁₂)alkyl, —(C₁-C₆)alkyl-OR⁴, —(C₁-C₆)alkyl-O—(C₁-C₆)alkyl, —C(O)R⁵, —(CH₂)_nNR⁷R⁸, and —(CH₂)_nN⁺(R⁴)₃, wherein when W is O, R¹ and R² can optionally be taken together with the O and N to which they are respectively joined to form a 4 to 8 membered heterocyclyl ring, wherein the heterocyclyl ring may be optionally substituted by one to two R¹¹ groups;

R³ is selected from the group consisting of hydrogen, (C₁-C₁₂)alkyl, —NR¹R², —OR⁵,



wherein:

X is a monocyclic or bicyclic (C₅-C₁₄)aryl,

Y is selected from a monocyclic or bicyclic (C₂-C₉)heterocyclyl

or monocyclic or bicyclic (C₂-C₉)heteroaryl, each having one to three heteroatoms selected from S, N or O, and

Z is a monocyclic or bicyclic (C₃-C₈)cycloalkyl;

R² and R³ can optionally be taken together with the nitrogen and L₂ to which they are respectively joined to form a 4 to 8 membered heterocyclyl ring, wherein the heterocyclyl ring may be optionally substituted by one to two R¹¹ groups;

R⁴ is selected from the group consisting of —H and (C₁-C₆)alkyl;

R⁵ is selected from the group consisting of —H, (C₁-C₆)alkyl, —R³, —(CH₂)_nNR⁷R⁸, and —(CH₂)_nOR⁷.

R⁶ and R⁶ⁱ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, (C₁-C₆)alkoxy, haloalkyl, —Y, —(CH₂)_nNR⁷R⁸, —C(O)OH, and —C(O)NH₂, wherein the R⁶ and R⁶ⁱ groups can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring, and wherein the cycloalkyl ring may be optionally substituted by one to three R¹¹ groups;

R⁷ and R⁸ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, —Q-aryl(R⁴)_n, —NR¹⁴R¹⁵, —C(O)CH₃, wherein R⁷ and R⁸ can optionally be taken together with the nitrogen to which they are joined to form a 4 to 8 membered heterocyclyl or heteroaryl ring containing one to three heteroatoms selected from —NR⁵—, —O—, —S—, —S(O)—, or —SO₂—, wherein the heterocyclyl or heteroaryl ring may be optionally substituted by one to three R¹¹ groups;

R⁹ is halo;

R¹⁰ is —N(R¹⁶)₂;

R¹¹, R¹², and R¹³ are independently selected from the group consisting of oxo, hydroxyl, halo, (C₁-C₆)alkoxy, —R⁶(R⁹)_q, —OR⁶(R⁹)_q, —SO₂R⁶, (C₁-C₆)alkyl, —C(O)R¹⁰, —R⁴YR⁶, —CO(O)R⁴, and —CO(O)R⁵, wherein any two R¹¹, R¹² or R¹³ groups can optionally join to form a 3 to 8 membered cycloalkyl, aryl, heterocyclyl or heteroaryl ring, wherein the heterocyclyl or heteroaryl ring may contain one to three heteroatoms selected from —NR⁵—, —O—, —S—, —S(O)—, or —SO₂—, and wherein the cycloalkyl, aryl, heterocyclyl or heteroaryl ring may be optionally substituted by one to three R¹⁶ groups;

R¹⁴ and R¹⁵ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, (C₁-C₆)alkoxy, —[C(R⁹)₂]_r, —O[C(R⁹)₂]_r, Oxo, hydroxyl, halo, —C(O)R⁷, —R¹⁰, and —CO(O)R², wherein R¹⁴ and R¹⁵ can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring or 4 to 8 membered heterocyclyl ring containing one to three heteroatoms selected from —NR⁵—, —O—, —S—, —S(O)—, or —SO₂—, wherein the cycloalkyl ring or heterocyclyl ring may be optionally substituted by one to three R¹⁶ groups;

R¹⁶ is independently selected from the group consisting of —H, halo, oxo, hydroxyl, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₃-C₈)cycloalkyl, —R⁶(R⁹)_q, —OR⁶(R⁹)_q, —N(R⁴)₂, —(CH₂)_n-heterocyclyl, —C(O)OH, —C(O)NH₂, —R⁵(R⁹)_q, —OR⁵(R⁹)_q, nitro, —SO₂R⁶, —C(O)R¹⁰, and —CO(O)R⁴;

m and n in each instance are independently 0, 1, 2, 3, or 4; p is independently 0, 1, 2, 3, or 4; and

r and q in each instance are independently 0, 1, 2, 3, or 4.

In a second aspect, the present invention relates to a pharmaceutical composition comprising a) the compound of Formula I or Formula II or a pharmaceutically acceptable salt thereof; and b) a pharmaceutically acceptable excipient.

In a third aspect, the present invention is a method of treating an HIV infection comprising administering to a subject suffering therefrom a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof.

Compounds of the present invention are useful for the treatment of subjects with an HIV infection or for the treatment of subjects at risk of acquiring an HIV infection.

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BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 shows a bar graph representing a comparison between Bevirimat and compound 51 of their relative ability to inhibit HIV reverse transcriptase activity across a broad panel of HIV-1 isolates.

FIG. 2 shows a bar graph representing a comparison between compound 51 and compound C of their relative ability to inhibit HIV reverse transcriptase activity across a broad panel of HIV-1 isolates.

FIG. 3 shows a line graph representing an extrapolation of Bevirimat normalized IC_{50} values to 100% human serum.

FIG. 4 shows a line graph representing an extrapolation of compound B normalized IC_{50} values to 100% human serum.

FIG. 5 shows a line graph representing an extrapolation of compound 51 normalized IC_{50} values to 100% human serum.

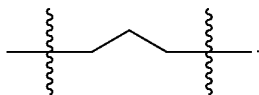
DETAILED DESCRIPTION OF REPRESENTATIVE EMBODIMENTS

Throughout this application, references are made to various embodiments relating to compounds, compositions, and methods. The various embodiments described are meant to provide a variety of illustrative examples and should not be construed as descriptions of alternative species. Rather it should be noted that the descriptions of various embodiments provided herein may be of overlapping scope. The embodiments discussed herein are merely illustrative and are not meant to limit the scope of the present invention.

It is to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to limit the scope of the present invention. In this specification and in the claims that follow, reference will be made to a number of terms that shall be defined to have the following meanings.

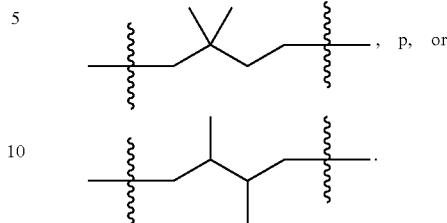
As used herein unless otherwise specified, “alkyl” refers to a monovalent saturated aliphatic hydrocarbyl group having from 1 to 14 carbon atoms and, in some embodiments, from 1 to 6 carbon atoms. “ (C_x-C_y) alkyl” refers to alkyl groups having from x to y carbon atoms. The term “alkyl” includes, by way of example, linear and branched hydrocarbyl groups such as methyl (CH_3-), ethyl (CH_3CH_2-), n-propyl ($CH_3CH_2CH_2-$), isopropyl ($((CH_3)_2CH-$), n-butyl ($CH_3CH_2CH_2CH_2-$), isobutyl ($((CH_3)_2CHCH_2-$), sec-butyl ($((CH_3)(CH_3CH_2)CH-$), t-butyl ($((CH_3)_3C-$), n-pentyl ($CH_3CH_2CH_2CH_2CH_2-$), and neopentyl ($(CH_3)_3CCH_2-$).

“Alkylene” or “alkylene” refers to divalent saturated aliphatic hydrocarbyl groups having from 1 to 10 carbon atoms and, in some embodiments, from 1 to 6 carbon atoms. “ (C_u-C_v) alkylene” refers to alkylene groups having from u to v carbon atoms. The alkylene groups include branched and straight chain hydrocarbyl groups. For example, “ (C_1-C_6) alkylene” is meant to include methylene, ethylene, propylene, 2-methylpropylene, dimethylethylene, pentylene, and so forth. As such, the term “propylene” could be exemplified by the following structure:



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Likewise, the term “dimethylbutylene” could be exemplified by any of the following three structures or more:



Furthermore, the term “ (C_1-C_6) alkylene” is meant to include such branched chain hydrocarbyl groups as cyclopropylmethylene, which could be exemplified by the following structure:



“Alkenyl” refers to a linear or branched hydrocarbyl group having from 2 to 10 carbon atoms and in some embodiments from 2 to 6 carbon atoms or 2 to 4 carbon atoms and having at least 1 site of vinyl unsaturation ($>C=C<$). For example, “ (C_x-C_y) alkenyl” refers to alkenyl groups having from x to y carbon atoms and is meant to include for example, ethenyl, propenyl, isopropylene, 1,3-butadienyl, and the like.

“Alkynyl” refers to a linear monovalent hydrocarbon radical or a branched monovalent hydrocarbon radical containing at least one triple bond. The term “alkynyl” is also meant to include those hydrocarbyl groups having one triple bond and one double bond. For example, “ (C_2-C_6) alkynyl” is meant to include ethynyl, propynyl, and the like.

“Alkoxy” refers to the group $-O$ -alkyl wherein alkyl is defined herein. Alkoxy includes, by way of example, methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, t-butoxy, sec-butoxy, and n-pentoxy.

“Acyl” refers to the groups $H-C(O)-$, $alkyl-C(O)-$, $alkenyl-C(O)-$, $alkynyl-C(O)-$, $cycloalkyl-C(O)-$, $aryl-C(O)-$, $heteroaryl-C(O)-$, and $heterocyclic-C(O)-$. Acyl includes the “acetyl” group $CH_3C(O)-$.

“Acylamino” refers to the groups $-NR^{20}C(O)alkyl$, $-NR^{20}C(O)cycloalkyl$, $-NR^{20}C(O)alkenyl$, $-NR^{20}C(O)alkynyl$, $-NR^{20}C(O)aryl$, $-NR^{20}C(O)heteroaryl$, and $-NR^{20}C(O)heterocyclic$, wherein R^{20} is hydrogen or alkyl.

“Acyloxy” refers to the groups $alkyl-C(O)O-$, $alkenyl-C(O)O-$, $alkynyl-C(O)O-$, $aryl-C(O)O-$, $cycloalkyl-C(O)O-$, $heteroaryl-C(O)O-$, and $heterocyclic-C(O)O-$.

“Amino” refers to the group $-NR^{21}R^{22}$ where R^{21} and R^{22} are independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, heterocyclic, $-SO_2$ -alkyl, $-SO_2$ -alkenyl, $-SO_2$ -cycloalkyl, $-SO_2$ -aryl, $-SO_2$ -heteroaryl, and $-SO_2$ -heterocyclic, and wherein R^{21} and R^{22} are optionally joined together with the nitrogen bound thereto to form a heterocyclic group.

When R^{21} is hydrogen and R^{22} is alkyl, the amino group is sometimes referred to herein as alkylamino. When R^{21} and R^{22} are alkyl, the amino group is sometimes referred to herein as dialkylamino. When referring to a monosubstituted amino, it is meant that either R^{21} or R^{22} is hydrogen but not both. When referring to a disubstituted amino, it is meant that neither R^{21} nor R^{22} are hydrogen.

“Hydroxyamino” refers to the group $-NHOH$.

“Alkoxyamino” refers to the group $-NHO$ -alkyl wherein alkyl is defined herein.

“Aminocarbonyl” refers to the group $-C(O)NR^{26}R^{27}$ where R^{26} and R^{27} are independently selected from hydrogen,

alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, heterocyclic, hydroxy, alkoxy, amino, and acylamino, and where R^{26} and R^{27} are optionally joined together with the nitrogen bound thereto to form a heterocyclic group.

“Aryl” refers to an aromatic group of from 6 to 14 carbon atoms and no ring heteroatoms and having a single ring (e.g., phenyl) or multiple condensed (fused) rings (e.g., naphthyl or anthryl). For multiple ring systems, including fused, bridged, and spiro ring systems having aromatic and non-aromatic rings that have no ring heteroatoms, the term “Aryl” or “Ar” applies when the point of attachment is at an aromatic carbon atom (e.g., 5,6,7,8 tetrahydronaphthalene-2-yl is an aryl group as its point of attachment is at the 2-position of the aromatic phenyl ring).

“AUC” refers to the area under the plot of plasma concentration of drug (not logarithm of the concentration) against time after drug administration.

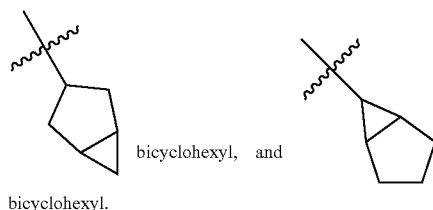
“ EC_{50} ” refers to the concentration of a drug that gives half-maximal response.

“ IC_{50} ” refers to the half-maximal inhibitory concentration of a drug. Sometimes, it is also converted to the pIC_{50} scale ($-\log IC_{50}$), in which higher values indicate exponentially greater potency.

“Clade” refers to a hypothetical construct based on experimental data. Clades are found using multiple (sometimes hundreds) of traits from a number of species (or specimens) and analyzing them statistically to find the most likely phylogenetic tree for the group.

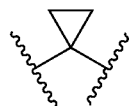
“Cyano” or “nitrile” refers to the group $—CN$.

“Cycloalkyl” refers to a saturated or partially saturated cyclic group of from 3 to 14 carbon atoms and no ring heteroatoms and having a single ring or multiple rings including fused, bridged, and spiro ring systems. For multiple ring systems having aromatic and non-aromatic rings that have no ring heteroatoms, the term “cycloalkyl” applies when the point of attachment is at a non-aromatic carbon atom (e.g., 5,6,7,8-tetrahydronaphthalene-5-yl). The term “Cycloalkyl” includes cycloalkenyl groups, such as cyclohexenyl. Examples of cycloalkyl groups include, for instance, adamantyl, cyclopropyl, cyclobutyl, cyclohexyl, cyclopentyl, cyclooctyl, cyclopentenyl, and cyclohexenyl. Examples of cycloalkyl groups that include multiple bicycloalkyl ring systems are bicyclohexyl, bicyclopentyl, bicyclooctyl, and the like. Two such bicycloalkyl multiple ring structures are exemplified and named below:

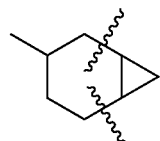


“(C_uC_v)cycloalkyl” refers to cycloalkyl groups having u to v carbon atoms.

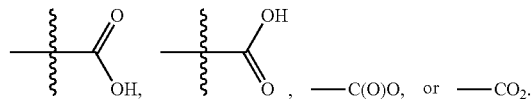
“Spiro cycloalkyl” refers to a 3 to 10 member cyclic substituent formed by replacement of two hydrogen atoms at a common carbon atom in a cyclic ring structure or in an alkylene group having 2 to 9 carbon atoms, as exemplified by the following structure wherein the group shown here attached to bonds marked with wavy lines is substituted with a spiro cycloalkyl group:



“Fused cycloalkyl” refers to a 3 to 10 member cyclic substituent formed by the replacement of two hydrogen atoms at different carbon atoms in a cycloalkyl ring structure, as exemplified by the following structure wherein the cycloalkyl group shown here contains bonds marked with wavy lines which are bonded to carbon atoms that are substituted with a fused cycloalkyl group:



“Carboxy” or “carboxyl” refers interchangeably to the groups



“Halo” or “halogen” refers to fluoro, chloro, bromo, and iodo.

“Haloalkyl” refers to substitution of an alkyl group with 1 to 3 halo groups (e.g., bifluoromethyl or trifluoromethyl).

“Haloalkoxy” refers to substitution of alkoxy groups with 1 to 5 (e.g. when the alkoxy group has at least 2 carbon atoms) or in some embodiments 1 to 3 halo groups (e.g. trifluoromethoxy).

“Human Serum Protein Shift Assay” refers to an HIV assay using a Luciferase Reporter to determine percent inhibition— pIC_{50} . The HIV assay makes use of a two-cell co-culture system. In this assay, an infected cell line J4HxB2 and an indicator cell line HOS (delta LTR+Luciferase) are co-cultured in the presence and absence of compound. The assay is designed to find inhibitors that prevent the infection of HOS cells by the J4HxB2 cell line. The assay can detect inhibitors of any stage of the HIV infection cycle.

“Hydroxy” or “hydroxyl” refers to the group $—OH$.

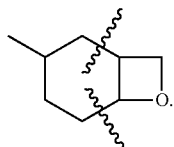
“Heteroaryl” refers to an aromatic group of from 1 to 14 carbon atoms and 1 to 6 heteroatoms selected from oxygen, nitrogen, and sulfur and includes single ring (e.g. imidazolyl) and multiple ring systems (e.g. benzimidazol-2-yl and benzimidazol-6-yl). For multiple ring systems, including fused, bridged, and spiro ring systems having aromatic and non-aromatic rings, the term “heteroaryl” applies if there is at least one ring heteroatom and the point of attachment is at an atom of an aromatic ring (e.g. 1,2,3,4-tetrahydroquinolin-6-yl and 5,6,7,8-tetrahydroquinolin-3-yl). In some embodiments, the nitrogen and/or the sulfur ring atom(s) of the heteroaryl group are optionally oxidized to provide for the N-oxide ($N \rightarrow O$), sulfinyl, or sulfonyl moieties. More specifically the term heteroaryl includes, but is not limited to, pyridyl, furanyl, thienyl, thiazolyl, isothiazolyl, triazolyl, imidazolyl, imidazolynyl, isoxazolyl, pyrrolyl, pyrazolyl, pyridazinyl, pyrimidinyl, purinyl, phthalazyl, naphthylpyridyl, benzofuranlyl, tetrahydrobenzofuranlyl, isobenzofuranlyl, benzothiazolyl, benzisothiazolyl, benzotriazolyl, indolyl, isoindolyl, indolizynyl, dihydroindolyl, indazolyl, indolynyl, benzoxazolyl,

quinolyl, isoquinolyl, quinolizyl, quianazolyl, quinoxalyl, tetrahydroquinolyl, isoquinolyl, quinazolinonyl, benzimidazolyl, benzisoxazolyl, benzothienyl, benzopyridazinyl, pteridyl, carbazolyl, carbolinyl, phenanthridinyl, acridinyl, phenanthrolinyl, phenazinyl, phenoxazinyl, phenothiazinyl, and phthalimidyl.

"Heterocyclic" or "heterocycle" or "heterocycloalkyl" or "heterocyclyl" refers to a saturated or partially saturated cyclic group having from 1 to 14 carbon atoms and from 1 to 6 heteroatoms selected from nitrogen, sulfur, phosphorus or oxygen and includes single ring and multiple ring systems including fused, bridged, and spiro ring systems. For multiple ring systems having aromatic and/or non-aromatic rings, the terms "heterocyclic", "heterocycle", "heterocycloalkyl", or "heterocyclyl" apply when there is at least one ring heteroatom and the point of attachment is at an atom of a non-aromatic ring (e.g. 1,2,3,4-tetrahydroquinoline-3-yl, 5,6,7,8-tetrahydroquinoline-6-yl, and decahydroquinolin-6-yl). In one embodiment, the nitrogen, phosphorus and/or sulfur atom(s) of the heterocyclic group are optionally oxidized to provide for the N-oxide, phosphinane oxide, sulfinyl, sulfonyl moieties. More specifically the heterocyclyl includes, but is not limited to, tetrahydropyryl, piperidinyl, piperazinyl, 3-pyrrolidinyl, 2-pyrrolidon-1-yl, morpholinyl, and pyrrolidinyl. A prefix indicating the number of carbon atoms (e.g., C₃-C₁₀) refers to the total number of carbon atoms in the portion of the heterocyclyl group exclusive of the number of heteroatoms.

Examples of heterocycle and heteroaryl groups include, but are not limited to, azetidine, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, pyridone, indolizine, isoindole, indole, dihydroindole, indazole, purine, quinolizine, isoquinoline, quinoline, phthalazine, naphthylpyridine, quinoxaline, quinazoline, cinnoline, pteridine, carbazole, carboline, phenanthridine, acridine, phenanthroline, isothiazole, phenazine, isoxazole, phenoxazine, phenothiazine, imidazolidine, imidazoline, piperidine, piperazine, indoline, phthalimide, 1,2,3,4-tetrahydroisoquinoline, 4,5,6,7-tetrahydrobenzo[b]thiophene, thiazole, thiazolidine, thiophene, benzo[b]thiophene, morpholine, thiomorpholine (also referred to as thiamorpholine), piperidine, pyrrolidine, and tetrahydrofuran.

"Fused heterocyclic" or "fused heterocycle" refer to a 3 to 10 member cyclic substituent formed by the replacement of two hydrogen atoms at different carbon atoms in a cycloalkyl ring structure, as exemplified by the following structure wherein the cycloalkyl group shown here contains bonds marked with wavy lines which are bonded to carbon atoms that are substituted with a fused heterocyclic group:

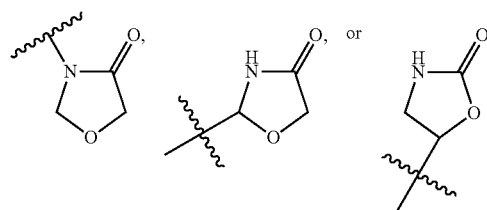


"Compound", "compounds", "chemical entity", and "chemical entities" as used herein refers to a compound encompassed by the generic formulae disclosed herein, any subgenus of those generic formulae, and any forms of the compounds within the generic and subgeneric formulae, including the racemates, stereoisomers, and tautomers of the compound or compounds.

The term "heteroatom" means nitrogen, oxygen, or sulfur and includes any oxidized form of nitrogen, such as N(O) {N⁺—O⁻} and sulfur such as S(O) and S(O)₂, and the quaternized form of any basic nitrogen.

"Oxazolidinone" refers to a 5-membered heterocyclic ring containing one nitrogen and one oxygen as heteroatoms and

also contains two carbons and is substituted at one of the two carbons by a carbonyl group as exemplified by any of the following structures, wherein the oxazolidinone groups shown here are bonded to a parent molecule, which is indicated by a wavy line in the bond to the parent molecule:



"Oxo" refers to a (=O) group.

"Polymorphism" refers to when two or more clearly different phenotypes exist in the same population of a species where the occurrence of more than one form or morph. In order to be classified as such, morphs must occupy the same habitat at the same time and belong to a panmictic population (one with random mating).

"Protein binding" refers to the binding of a drug to proteins in blood plasma, tissue membranes, red blood cells and other components of blood.

"Protein shift" refers to determining a binding shift by comparing the EC₅₀ values determined in the absence and presence of human serum.

"QVT" refers to the amino acids at positions 369, 370, and 371, respectively in the Sp1 fragment of HIV-1 Gag.

"Racemates" refers to a mixture of enantiomers. In an embodiment of the invention, the compounds of Formula I, or pharmaceutically acceptable salts thereof, are enantiomerically enriched with one enantiomer wherein all of the chiral carbons referred to are in one configuration. In general, reference to an enantiomerically enriched compound or salt, is meant to indicate that the specified enantiomer will comprise more than 50% by weight of the total weight of all enantiomers of the compound or salt.

"Solvate" or "solvates" of a compound refer to those compounds, as defined above, which are bound to a stoichiometric or non-stoichiometric amount of a solvent. Solvates of a compound includes solvates of all forms of the compound. In certain embodiments, solvents are volatile, non-toxic, and/or acceptable for administration to humans in trace amounts. Suitable solvates include water.

"Stereoisomer" or "stereoisomers" refer to compounds that differ in the chirality of one or more stereocenters. Stereoisomers include enantiomers and diastereomers.

"Tautomer" refer to alternate forms of a compound that differ in the position of a proton, such as enol-keto and imine-enamine tautomers, or the tautomeric forms of heteroaryl groups containing a ring atom attached to both a ring —NH— moiety and a ring =N— moiety such as pyrazoles, imidazoles, benzimidazoles, triazoles, and tetrazoles.

The term "atropisomer" refers to a stereoisomer resulting from an axis of asymmetry. This can result from restricted rotation about a single bond where the rotational barrier is high enough to allow differentiation of the isomeric species up to and including complete isolation of stable non-interconverting diastereomer or enantiomeric species. One skilled in the art will recognize that upon installing a nonsymmetrical R^x to core, the formation of atropisomers is possible. In addition, once a second chiral center is installed in a given molecule containing an atropisomer, the two chiral elements taken together can create diastereomeric and enantiomeric stereochemical species. Depending upon the substitution about the C_x axis, interconversion between the atropisomers may or may not be possible and may depend on temperature.

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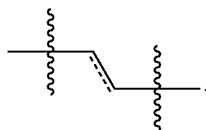
In some instances, the atropisomers may interconvert rapidly at room temperature and not resolve under ambient conditions. Other situations may allow for resolution and isolation but interconversion can occur over a period of seconds to hours or even days or months such that optical purity is degraded measurably over time. Yet other species may be completely restricted from interconversion under ambient and/or elevated temperatures such that resolution and isolation is possible and yields stable species. When known, the resolved atropisomers were named using the helical nomenclature. For this designation, only the two ligands of highest priority in front and behind the axis are considered. When the turn priority from the front ligand 1 to the rear ligand 1 is clockwise, the configuration is P, if counterclockwise it is M.

"Pharmaceutically acceptable salt" refers to pharmaceutically acceptable salts derived from a variety of organic and inorganic counter ions well known in the art and include, by way of example only, sodium, potassium, calcium, magnesium, ammonium, and tetraalkylammonium, and when the molecule contains a basic functionality, salts of organic or inorganic acids, such as hydrochloride, hydrobromide, tartrate, mesylate, acetate, maleate, and oxalate. Suitable salts include those described in P. Heinrich Stahl, Camille G. Wermuth (Eds.), *Handbook of Pharmaceutical Salts Properties, Selection, and Use*; 2002.

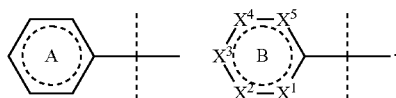
"Patient" or "subject" refers to mammals and includes humans and non-human mammals.

"Treating" or "treatment" of a disease in a patient refers to 1) preventing the disease from occurring in a patient that is predisposed or does not yet display symptoms of the disease; 2) inhibiting the disease or arresting its development; or 3) ameliorating or causing regression of the disease.

Wherever dashed lines occur adjacent to single bonds denoted by solid lines, then the dashed line represents an optional double bond at that position. Likewise, wherever dashed circles appear within ring structures denoted by solid lines or solid circles, then the dashed circles represent one to three optional double bonds arranged according to their proper valence taking into account whether the ring has any optional substitutions around the ring as will be known by one of skill in the art. For example, the dashed line in the structure below could either indicate a double bond at that position or a single bond at that position:



Similarly, ring A below could be a cyclohexyl ring without any double bonds or it could also be a phenyl ring having three double bonds arranged in any position that still depicts the proper valence for a phenyl ring. Likewise, in ring B below, any of X¹-X⁵ could be selected from: C, CH, or CH₂, N, or NH, and the dashed circle means that ring B could be a cyclohexyl or phenyl ring or a N-containing heterocycle with no double bonds or a N-containing heteroaryl ring with one to three double bonds arranged in any position that still depicts the proper valence:

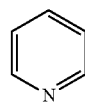


Where specific compounds or generic formulas are drawn that have aromatic rings, such as aryl or heteroaryl rings, then

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it will be understood by one of skill in the art that the particular aromatic location of any double bonds are a blend of equivalent positions even if they are drawn in different locations from compound to compound or from formula to formula.

For example, in the two pyridine rings (A and B) below, the double bonds are drawn in different locations, however, they are known to be the same structure and compound:



The present invention includes compounds as well as their pharmaceutically acceptable salts. Accordingly, the word "or" in the context of "a compound or a pharmaceutically acceptable salt thereof" is understood to refer to either: 1) a compound alone or a compound and a pharmaceutically acceptable salt thereof (alternative), or 2) a compound and a pharmaceutically acceptable salt thereof (in combination).

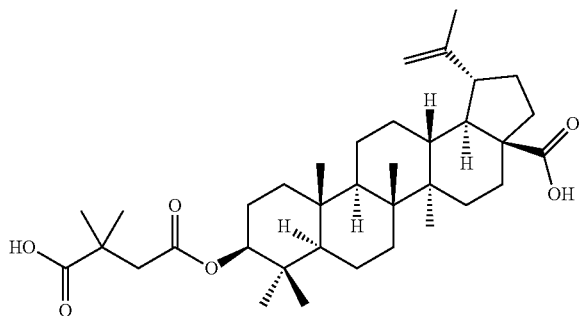
Unless indicated otherwise, the nomenclature of substituents that are not explicitly defined herein are arrived at by naming the terminal portion of the functionality followed by the adjacent functionality toward the point of attachment. For example, the substituent "arylkalkyloxycarbonyl" refers to the group (aryl)-(alkyl)-O-C(O)-. In a term such as "-C(R^x)₂", it should be understood that the two R^x groups can be the same, or they can be different if R^x is defined as having more than one possible identity. In addition, certain substituents are drawn as -R^xR^y, where the "-" indicates a bond adjacent to the parent molecule and R^y being the terminal portion of the functionality. Similarly, it is understood that the above definitions are not intended to include impermissible substitution patterns (e.g., methyl substituted with 5 fluoro groups). Such impermissible substitution patterns are well known to the skilled artisan.

As recited above, Bevirimat is a yet unapproved anti-HIV drug derived from a betulinic acid-like compound, first isolated from *Syzygium claviflorum*, a Chinese herb. It is believed to inhibit HIV by a novel mechanism, so-called maturation inhibition. Like protease inhibitors, Bevirimat and other maturation inhibitors interfere with protease processing of newly translated HIV polyprotein precursor, called gag. Gag is an essential structural protein of the HIV virus. Gag undergoes a chain of interactions both with itself and with other cellular and viral factors to accomplish the assembly of infectious virus particles.

However, naturally occurring polymorphisms in HIV are present in some infected individuals, thus lowering the anti-HIV efficacy of some currently considered therapies. Indeed, studies have shown that presence of a number of single nucleotide polymorphisms in the Capsid/SP1 spacer protein (CA/SP1) cleavage site has resulted in clinical resistance in HIV patients to Bevirimat. Likewise, mutations in the glutamine-valine-threonine (QVT) motif of the SP1 peptide are also known to cause Bevirimat resistance in HIV infected patients. Mutations in the QVT motif of the SP1 peptide are the primary predictors of failure to respond to Bevirimat and the effect of these mutations has been repeatedly demonstrated. These problems eventually led to the cessation of clinical development of Bevirimat. See Knapp, D., et al., *J. Clin. Microbiol.* 49 (1): 201-208 (2011).

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Bevirimat:



Bevirimat's Clinical Problems:

Polymorphism issues & weak potency.

MT4 antiviral assay NL4-3 strain EC_{50} =223 nM.MT4 antiviral assay NL4-3 strain with V370A site directed mutant polymorphism EC_{50} =6062 nM.

In assay fold shift with human serum 157 fold. See Table 6.

 C_{min} target >20 μ g/mL*.

>40% of clade B patients have QVT polymorphisms*.

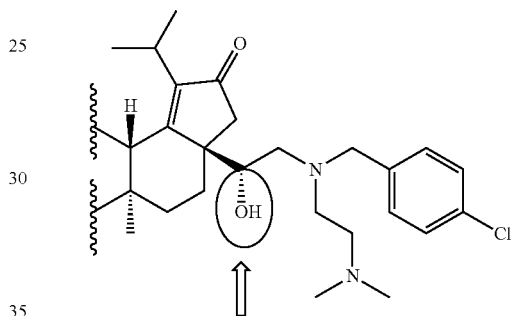
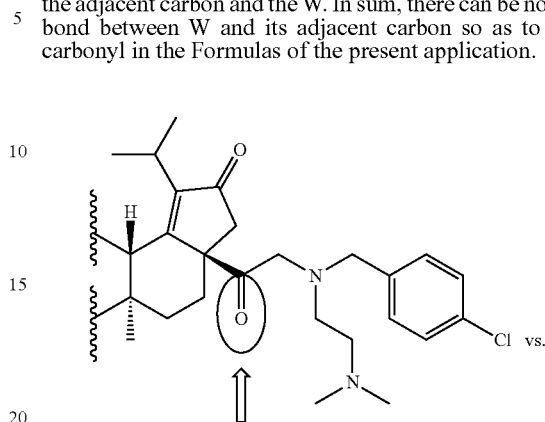
*See McCallister, et al., XVII International Drug Resistance Workshop, Jun. 10-14, 2008, Sitges, Spain. Conference poster "HIV-1 Gag Polymorphisms Determine Treatment Response to Bevirimat (PA-457)".

After the above HIV clinical problems with Bevirimat were reported, several new HIV active maturation inhibitor compounds were discovered. For example, certain maturation inhibitor compounds (hereinafter, compounds "A", "B" and "C", as shown below) have been described in PCT Published Application No. WO2011/100308 and PCT Application Serial No. PCT/CN2011/001302. In addition, the present application also describes compounds 51 and 56, among others, as detailed throughout. The present application describes compounds that are novel over the compounds described in PCT Published Application No. WO2011/100308 and PCT Application Serial No. PCT/CN2011/001302. In addition, certain compounds described herein show unexpectedly superior properties over the compounds ("A", "B", and "C") described in PCT Published Application No. WO2011/100308 and PCT Application Serial No. PCT/CN2011/001302.

One difference between the compounds described in those two references and the compounds of the present application is that both of those references have compounds requiring a carbonyl group at a position where, instead, the present application describes compounds that cannot have a carbonyl at the same position. By way of example only, this carbonyl

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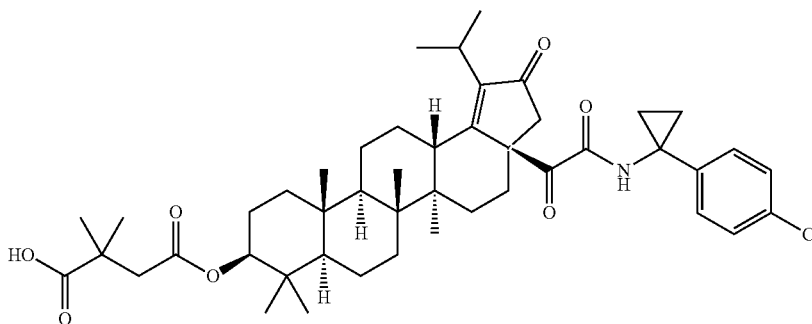
versus non-carbonyl difference is highlighted by the arrows indicated directly below. The generic structures of Formulas (I) and (II) bear this out within the present application because when W is oxygen, there can only be a single bond between the adjacent carbon and the W. In sum, there can be no double bond between W and its adjacent carbon so as to form a carbonyl in the Formulas of the present application.



Indeed, this structural difference has now been discovered to unexpectedly improve many of the properties that are involved with creating an efficacious drug for the prevention and/or treatment of viral diseases, such as HIV. One or more of such properties of certain compounds described within the present application, include, but are not limited to, improving the HIV virus polymorphism coverage, improving the in vitro potency (EC_{50}), reducing the projected clinical human AUC target, potentially reducing any toxicity window by lowering the required dosage to be efficacious, and reducing the impact of protein binding and/or serum shift upon the projected clinical AUC target.

Such improvements to the pharmacokinetics and projected clinical use of certain compounds described herein are described in more detail within Examples 84-89 below.

Compound A

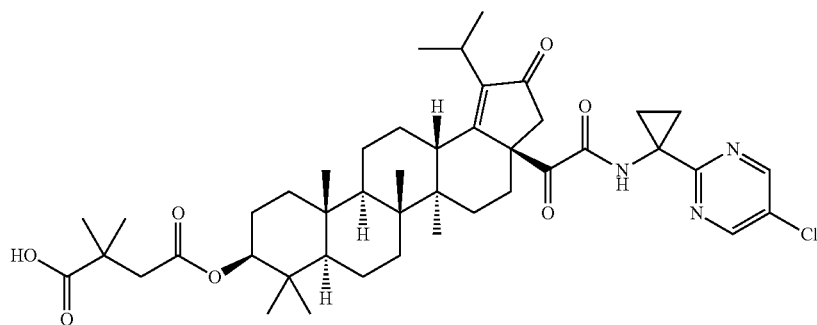


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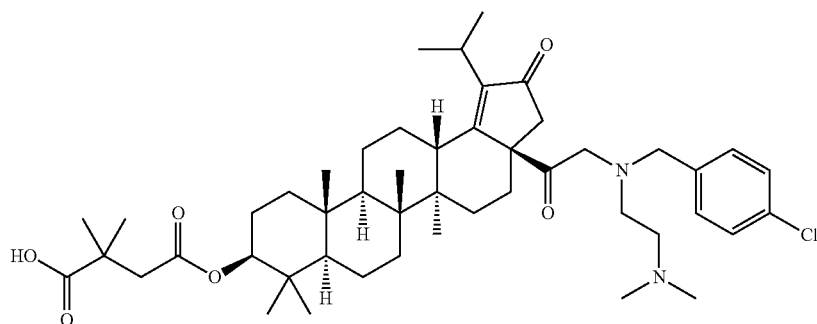
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-continued

Compound B

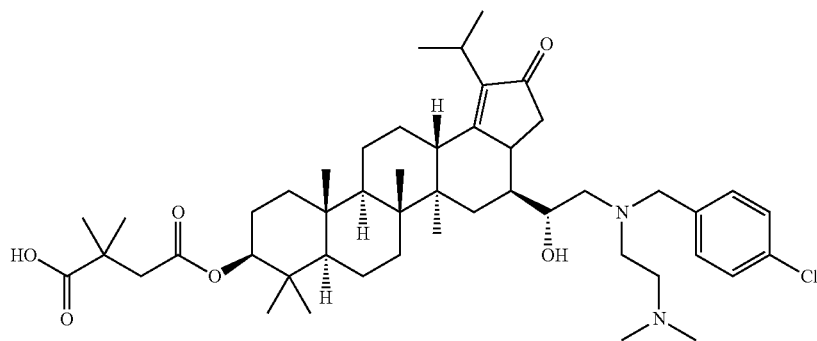


Compound C



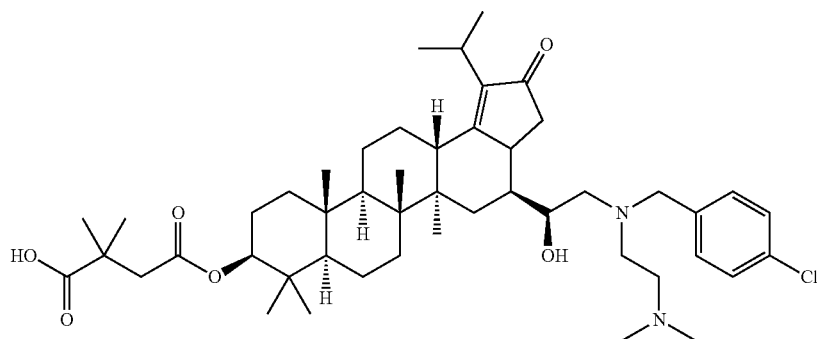
(Example 17-19 from PCT Published Application No. WO/2011/10038)

Compound 51



(Example 18 herein)

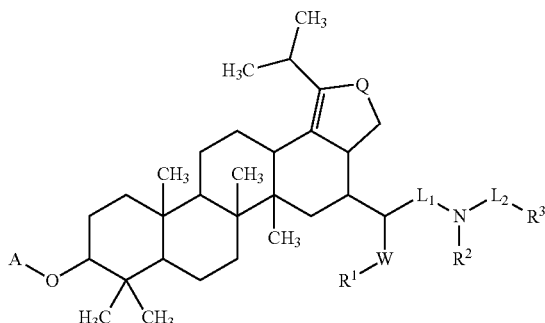
Compound 56



(Example 19 herein)

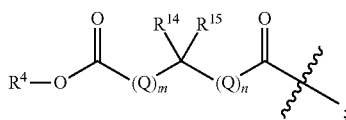
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In accordance with one embodiment of the present invention, there is provided a compound having the structure of Formula I:



or a pharmaceutically acceptable salt thereof, wherein:

A is

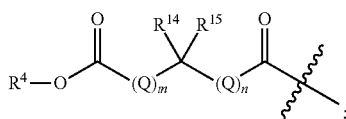


L_1 and L_2 are independently selected from a bond or $[C(R^9R^{10})]_q$;

each instance of Q is independently selected from $-CH_2-$ or $-C(=O)-$;

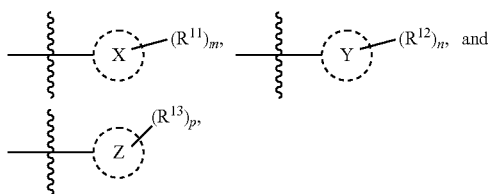
W is selected from a bond or O;

R^1 is selected from the group consisting of $-H$, (C_1-C_{12}) alkyl, $-C(O)R^5$, $-CH_2-O-(C_1-C_6)$ alkyl, 2-tetrahydro-2H-pyran, and



R^2 is selected from the group consisting of $-H$, (C_1-C_{12}) alkyl, $-(C_1-C_6)$ alkyl- OR^4 , $-(C_1-C_6)$ alkyl-O- (C_1-C_6) alkyl, $-C(O)R^5$, $-(CH_2)_rNR^7R^8$, and $-(CH_2)_rN^+(R^4)_3$, wherein when W is O, R^1 and R^2 can optionally be taken together with the O and N to which they are respectively joined to form a 4 to 8 membered heterocyclyl ring, wherein the heterocyclyl ring may be optionally substituted by one to two R^{11} groups;

R^3 is selected from the group consisting of $-H$, (C_1-C_{12}) alkyl, $-NR^1R^2$, $-OR^5$,



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wherein:

X is a monocyclic or bicyclic (C_5-C_{14}) aryl,

Y is selected from a monocyclic or bicyclic (C_2-C_9) heterocyclyl or monocyclic or bicyclic (C_2-C_9) heteroaryl, each having one to three heteroatoms selected from S, N or O, and

Z is a monocyclic or bicyclic (C_3-C_8) cycloalkyl;

R^2 and R^3 can optionally be taken together with the nitrogen and L_2 to which they are respectively joined to form a 4 to 8 membered heterocyclyl ring, wherein the heterocyclyl ring may be optionally substituted by one to two R^{11} groups;

R^4 is selected from the group consisting of $-H$ and (C_1-C_6) alkyl;

R^5 is selected from the group consisting of $-H$, (C_1-C_6) alkyl, $-R^3$, $-(CH_2)_rNR^7R^8$, and $-(CH_2)_rOR^7$.

R^6 and R^6 are independently selected from the group consisting of $-H$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, (C_1-C_6) alkoxy, haloalkyl, $-Y$, $-(CH_2)_rNR^7R^8$, $-C(O)OH$, and $-C(O)NH_2$, wherein the R^6 and R^6 groups can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring, and wherein the cycloalkyl ring may be optionally substituted by one to three R^{11} groups;

R^7 and R^8 are independently selected from the group consisting of $-H$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, $-Q$ -aryl- $(R^4)_n$, $-NR^{14}R^{15}$, $-C(O)CH_3$, wherein R^7 and R^8 can optionally be taken together with the nitrogen to which they are joined to form a 4 to 8 membered heterocyclyl or heteroaryl ring containing one to three heteroatoms selected from $-NR^5$, $-O$, $-S$, $-S(O)$, or $-SO_2$, wherein the heterocyclyl or heteroaryl ring may be optionally substituted by one to three R^{11} groups;

R^9 is halo;

R^{10} is $-N(R^{16})_2$;

R^{11} , R^{12} , and R^{13} are independently selected from the group consisting of oxo, hydroxyl, halo, (C_1-C_6) alkoxy, $-R^6(R^9)_q$, $-OR^6(R^9)_q$, nitro, $-SO_2R^6$, (C_1-C_6) alkyl, $-C(O)R^{10}$, $-R^4YR^6$, $-CO(O)R^4$, and $-CO(O)R^5$, wherein any two R^{11} , R^{12} or R^{13} groups can optionally join to form a 3 to 8 membered cycloalkyl, aryl, heterocyclyl or heteroaryl ring, wherein the heterocyclyl or heteroaryl ring may contain one to three heteroatoms selected from $-NR^5$, $-O$, $-S$, $-S(O)$, or $-SO_2$, and wherein the cycloalkyl, aryl, heterocyclyl or heteroaryl ring may be optionally substituted by one to three R^{16} groups;

R^{14} and R^{15} are independently selected from the group consisting of $-H$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, (C_1-C_6) alkoxy, $-[C(R^6)_2]_r$, $-O[C(R^6)_2]_r$, oxo, hydroxyl, halo, $-C(O)R^7$, $-R^{10}$, and $-CO(O)R^2$, wherein R^{14} and R^{15} can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring or 4 to 8 membered heterocyclyl ring containing one to three heteroatoms selected from $-NR^5$, $-O$, $-S$, $-S(O)$, or $-SO_2$, wherein the cycloalkyl ring or heterocyclyl ring may be optionally substituted by one to three R^{16} groups;

R^{16} is independently selected from the group consisting of $-H$, halo, oxo, hydroxyl, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_3-C_8) cycloalkyl, $-R^6(R^9)_q$, $-OR^6(R^9)_q$, $-N(R^4)_2$, $-(CH_2)_r$ -heterocycle, $-C(O)OH$, $-C(O)NH_2$, $-R^5(R^9)_q$, nitro, $-SO_2R^6$, $-C(O)R^{10}$, and $-CO(O)R^4$;

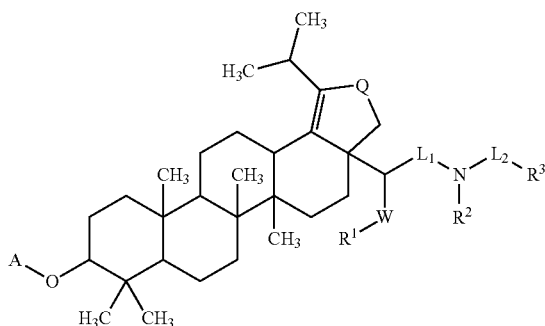
m and n in each instance are independently 0, 1, 2, 3, or 4;

p is independently 0, 1, 2, 3, or 4; and

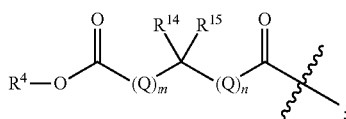
r and q in each instance are independently 0, 1, 2, 3, or 4.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I:

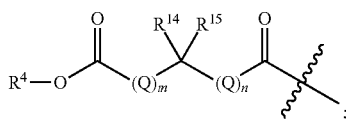
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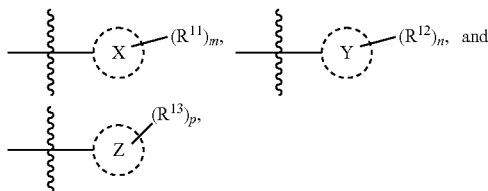
or a pharmaceutically acceptable salt thereof, wherein:
A is



L_1 and L_2 are $[C(R^6R^{6a})]_q$;
each Q is independently selected from $-CH_2-$ or $-C(=O)-$;
W is selected from a bond or O;
 R^1 is selected from the group consisting of $-H$, (C_1-C_6) alkyl, $-C(O)R^4$, and



R^2 is selected from the group consisting of $-H$, (C_1-C_6) alkyl, $-(C_1-C_6)alkyl-OR^4$, $-(C_1-C_6)alkyl-O-(C_1-C_6)alkyl$, $-C(O)R^5$, $-(CH_2)_rNR^7R^8$, and $-(CH_2)_rN^+(R^4)_3$;
 R^3 is selected from the group consisting of hydrogen, (C_1-C_{12}) alkyl, $-NR^1R^2$, $-OR^5$,



wherein:

X is a monocyclic or bicyclic (C_5-C_{14}) aryl;
Y is selected from a monocyclic or bicyclic (C_2-C_9) heterocyclyl or monocyclic or bicyclic (C_2-C_9) heteroaryl, each having one to three heteroatoms selected from S, N or O, and
Z is a monocyclic or bicyclic (C_3-C_8) cycloalkyl;
 R^4 is selected from the group consisting of $-H$ and (C_1-C_6) alkyl;
 R^5 is selected from the group consisting of (C_1-C_6) alkyl, $-(CH_2)_rNR^7R^8$, and $-(CH_2)_rOR^7$;
 R^6 and R^{6a} are independently selected from the group consisting of $-H$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, (C_1-C_6)

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alkoxy, haloalkyl, $-(CH_2)_rNR^7R^8$, $-C(O)OH$, and $-C(O)NH_2$, wherein the R^6 and R^{6a} groups can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring, and wherein the cycloalkyl ring may be optionally substituted by one to three R^{11} groups;

R^7 and R^8 are independently selected from the group consisting of $-H$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, $-NR^{14}R^{15}$, and $-C(O)CH_3$;

R^9 is halo;

R^{10} is $-N(R^{16})_2$;

R^{11} , R^{12} , and R^{13} are independently selected from the group consisting of oxo, hydroxyl, halo, (C_1-C_6) alkoxy, $-R^6(R^9)_q$, $-OR^6(R^9)_q$, nitro, $-SO_2R^6$, (C_1-C_6) alkyl, $-C(O)R^{10}$, $-R^4YR^6$, $-CO(O)R^4$, and $-CO(O)R^5$;

R^{14} and R^{15} are independently selected from the group consisting of $-H$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, (C_1-C_6) alkoxy, $-[C(R^6)_2]_r-$, $-O[C(R^6)_2]_r-$, oxo, hydroxyl, halo, $-C(O)R^7$, $-R^{10}$, and $-CO(O)R^2$;

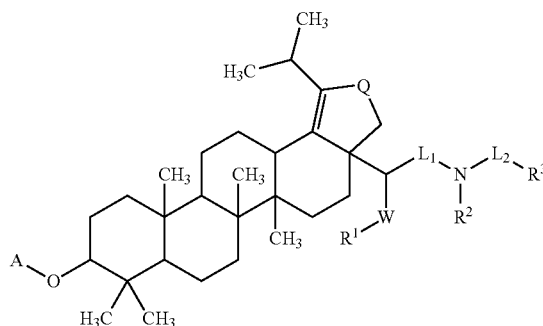
R^{16} is independently selected from the group consisting of $-H$, oxo, halo, hydroxyl, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_3-C_8) cycloalkyl, $-R^6(R^9)_q$, $-OR^6(R^9)_q$, $-N(R^4)_2$, $-(CH_2)_r$ -heterocycle, $-C(O)OH$, $-C(O)NH_2$, $-R^5(R^9)_q$, $-OR^5(R^9)_q$, nitro, $-SO_2R^6$, $-C(O)R^{10}$, and $-CO(O)R^4$;

m and n in each instance are independently 0, 1, 2, 3, or 4;

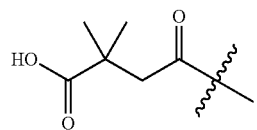
p is independently 0, 1, 2, 3, or 4; and

r and q in each instance are independently 0, 1, 2, 3, or 4.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I:



or a pharmaceutically acceptable salt thereof, wherein:
A is



L_1 and L_2 are both $(-CH_2-)$;

Q is $-C(=O)-$;

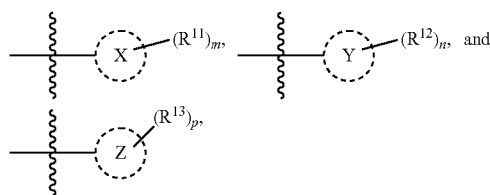
W is O;

R^1 is $-H$;

R^2 is selected from the group consisting of $-H$, (C_1-C_6) alkyl, $-(C_1-C_6)alkyl-OR^4$, $-(C_1-C_6)alkyl-O-(C_1-C_6)alkyl$, $-C(O)R^5$, and $-(CH_2)_rNR^7R^8$;

R^3 is selected from the group consisting of $-H$, (C_1-C_{12}) alkyl, $-NR^1R^2$, $-OR^5$,

21



wherein:

X is a monocyclic or bicyclic (C₅-C₁₄)aryl;

Y is selected from a monocyclic or bicyclic (C₂-C₈)heterocyclyl or monocyclic or bicyclic (C₂-C₈)heteroaryl, each having one to three heteroatoms selected from S, N or O, and

Z is a monocyclic or bicyclic (C₃-C₈)cycloalkyl;

R⁴ is selected from the group consisting of —H and (C₁-C₆)alkyl;

R⁵ is selected from the group consisting of (C₁-C₆)alkyl, —(CH₂)_rNR⁷R⁸, and —(CH₂)_rOR⁷;

R⁶ and R^{6a} are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, (C₁-C₆)alkoxy, haloalkyl, —(CH₂)_rNR⁷R⁸, —C(O)OH, and —C(O)NH₂;

R⁷ and R⁸ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, —NR¹⁴R¹⁵, and —C(O)CH₃;

R⁹ is halo;

R¹⁰ is —N(R¹⁶)₂;

R¹¹, R¹², and R¹³ are independently selected from the group consisting of oxo, hydroxyl, halo, (C₁-C₆)alkoxy, —R⁶(R⁹)_q, —OR⁶(R⁹)_q, nitro, —SO₂R⁶, (C₁-C₆)alkyl, —C(O)R¹⁰, —R⁴YR⁶, —CO(O)R⁴, and —CO(O)R⁵;

R¹⁴ and R¹⁵ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, (C₁-C₆)alkoxy, —[C(R⁶)₂]_r—, —O[C(R⁶)₂]_r—, oxo, hydroxyl, halo, —C(O)R⁷, —R¹⁰, and —CO(O)R²;

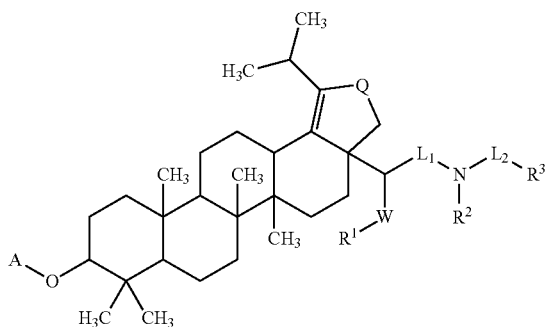
R¹⁶ is independently selected from the group consisting of —H, oxo, halo, hydroxyl, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₃-C₈)cycloalkyl, —R⁶(R⁹)_q, —OR⁶(R⁹)_q, —N(R⁴)₂, —(CH₂)_r-heterocyclyl, —C(O)OH, —C(O)NH₂, —R⁵(R⁹)_q, —OR⁵(R⁹)_q, nitro, —SO₂R⁶, —C(O)R¹⁰, and —CO(O)R⁴;

m and n in each instance are independently 0, 1, or 2;

p is independently 0, 1, or 2; and

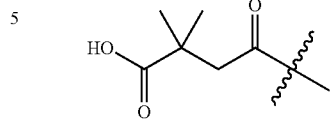
r and q in each instance are independently 0, 1, 2, or 3.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I:



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or a pharmaceutically acceptable salt thereof, wherein:
A is



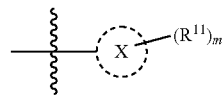
L₁ and L₂ are both (—CH₂—);
Q is —C(=O)—;

W is O;

R¹ is —H;

R² is selected from the group consisting of —H, (C₁-C₆)alkyl, —C(O)R⁵, and —(CH₂)_rNR⁶R⁸;

R³ is



wherein X is a monocyclic or bicyclic (C₅-C₁₄)aryl;

R⁴ is selected from the group consisting of —H and (C₁-C₆)alkyl;

R⁵ is selected from the group consisting of (C₁-C₆)alkyl, —(CH₂)_rNR⁷R⁸, and —(CH₂)_rOR⁷;

R⁶ is selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, (C₁-C₆)alkoxy, haloalkyl, —(CH₂)_rNR⁷R⁸, —C(O)OH, and —C(O)NH₂;

R⁷ and R⁸ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, —NR¹⁴R¹⁵, and —C(O)CH₃;

R⁹ is halo;

R¹⁰ is —N(R¹⁶)₂;

R¹¹, R¹², and R¹³ are independently selected from the group consisting of oxo, hydroxyl, halo, (C₁-C₆)alkoxy, —R⁶(R⁹)_q, —OR⁶(R⁹)_q, nitro, —SO₂R⁶, (C₁-C₆)alkyl, —C(O)R¹⁰, —R⁴YR⁶, and —CO(O)R⁵;

R¹⁴ and R¹⁵ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, (C₁-C₆)alkoxy, —[C(R⁶)₂]_r—, —O[C(R⁶)₂]_r—, oxo, hydroxyl, halo, —C(O)R⁷, —R¹⁰, and —CO(O)R²;

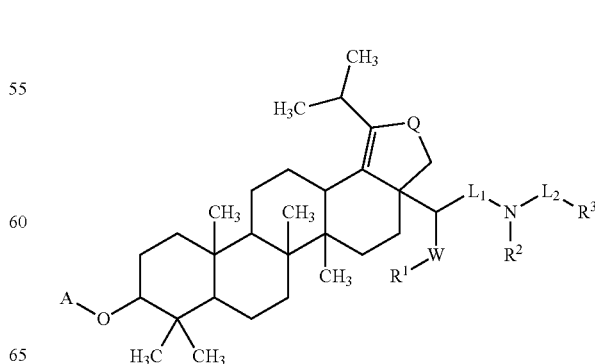
R¹⁶ is independently selected from the group consisting of —H, oxo, halo, hydroxyl, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₃-C₈)cycloalkyl, —R⁶(R⁹)_q, —OR⁶(R⁹)_q, —N(R⁴)₂, —(CH₂)_r-heterocyclyl, —C(O)OH, —C(O)NH₂, —R⁵(R⁹)_q, —OR⁵(R⁹)_q, nitro, —SO₂R⁶, —C(O)R¹⁰, and —CO(O)R⁴;

m and n in each instance are independently 0, 1, or 2;

p is independently 0, 1, or 2; and

r and q in each instance are independently 0, 1, 2, or 3.

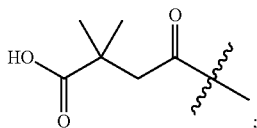
In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I:



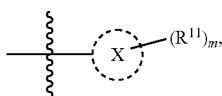
(I)

23

or a pharmaceutically acceptable salt thereof, wherein:
A is



L_1 and L_2 are both $(-\text{CH}_2-)$;
Q is $-\text{C}(=\text{O})-$;
W is O;
 R^1 is $-\text{H}$;
 R^2 is $-(\text{CH}_2)_r\text{NR}^7\text{R}^8$;
 R^3 is



wherein X is phenyl;

R^7 and R^8 are independently selected from the group consisting of $-\text{H}$ and methyl;

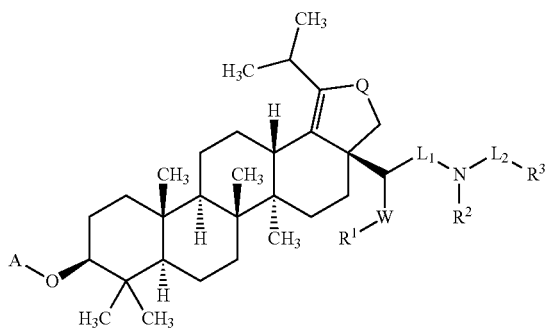
R^9 is selected from the group consisting of chloro, bromo, and fluoro;

R^{11} is selected from the group consisting of chloro, bromo, and fluoro;

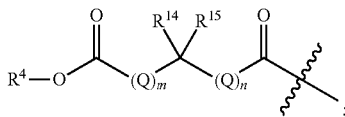
m is 0, 1, or 2; and

r is 1, 2, or 3.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula II:



or a pharmaceutically acceptable salt thereof, wherein:
A is



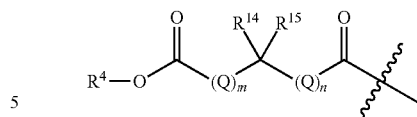
L_1 and L_2 are independently selected from a bond or $[\text{C}(\text{R}^6\text{R}^{6'})_q]$;

each instance of Q is independently selected from $-\text{CH}_2-$ or $-\text{C}(=\text{O})-$;

W is selected from a bond or O;

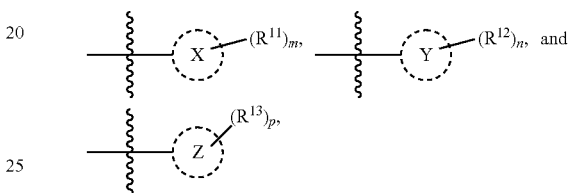
R^1 is selected from the group consisting of $-\text{H}$, $(\text{C}_1-\text{C}_{12})$ alkyl, $-\text{C}(\text{O})\text{R}^5$, $-\text{CH}_2-\text{O}-(\text{C}_1-\text{C}_6)$ alkyl, 2-tetrahydro-2H-pyran, and

24



R^2 is selected from the group consisting of $-\text{H}$, $(\text{C}_1-\text{C}_{12})$ alkyl, $-(\text{C}_1-\text{C}_6)$ alkyl- OR^4 , $-(\text{C}_1-\text{C}_6)$ alkyl- $\text{O}-(\text{C}_1-\text{C}_6)$ alkyl, $-\text{C}(\text{O})\text{R}^5$, $-(\text{CH}_2)_r\text{NR}^7\text{R}^8$, and $-(\text{CH}_2)_r\text{N}^+(\text{R}^4)_3$, wherein when W is O, R^1 and R^2 can optionally be taken together with the O and N to which they are respectively joined to form a 4 to 8 membered heterocyclyl ring, wherein the heterocyclyl ring may be optionally substituted by one to two R^{11} groups;

R^3 is selected from the group consisting of hydrogen, $(\text{C}_1-\text{C}_{12})$ alkyl, $-\text{NR}^1\text{R}^2$, $-\text{OR}^5$,



wherein:

X is a monocyclic or bicyclic $(\text{C}_5-\text{C}_{14})$ aryl;

Y is selected from a monocyclic or bicyclic (C_2-C_9) heterocyclyl or monocyclic or bicyclic (C_2-C_9) heteroaryl, each having one to three heteroatoms selected from S, N or O, and

Z is a monocyclic or bicyclic (C_3-C_8) cycloalkyl;

R^2 and R^3 can optionally be taken together with the nitrogen and L_2 to which they are respectively joined to form a 4 to 8 membered heterocyclyl ring, wherein the heterocyclyl ring may be optionally substituted by one to two R^{11} groups;

R^4 is selected from the group consisting of $-\text{H}$ and (C_1-C_6) alkyl;

R^5 is selected from the group consisting of $-\text{H}$, (C_1-C_6) alkyl, $-\text{R}^3$, $-(\text{CH}_2)_r\text{NR}^7\text{R}^8$, and $-(\text{CH}_2)_r\text{OR}^7$.

R^6 and $R^{6'}$ are independently selected from the group consisting of $-\text{H}$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, (C_1-C_6) alkoxy, haloalkyl, $-\text{Y}$, $-(\text{CH}_2)_r\text{NR}^7\text{R}^8$, $-\text{C}(\text{O})\text{OH}$, and $-\text{C}(\text{O})\text{NH}_2$, wherein the R^6 and $R^{6'}$ groups can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring, and wherein the cycloalkyl ring may be optionally substituted by one to three R^{11} groups;

R^7 and R^8 are independently selected from the group consisting of $-\text{H}$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, $-\text{Q}$ -aryl- $(\text{R}^4)_m$, $-\text{NR}^{14}\text{R}^{15}$, $-\text{C}(\text{O})\text{CH}_3$, wherein R^7 and R^8 can optionally be taken together with the nitrogen to which they are joined to form a 4 to 8 membered heterocyclyl or heteroaryl ring containing one to three heteroatoms selected from $-\text{NR}^5$, $-\text{O}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, or $-\text{SO}_2-$, wherein the heterocyclyl or heteroaryl ring may be optionally substituted by one to three R^{11} groups;

R^9 is halo;

R^{10} is $-\text{N}(\text{R}^{16})_2$;

R^{11} , R^{12} , and R^{13} are independently selected from the group consisting of oxo, hydroxyl, halo, (C_1-C_6) alkoxy, $-\text{R}^6$ $(\text{R}^9)_q$, $-\text{OR}^6(\text{R}^9)_q$, nitro, $-\text{SO}_2\text{R}^6$, (C_1-C_6) alkyl, $-\text{C}(\text{O})\text{R}^{10}$, $-\text{R}^4\text{YR}^6$, $-\text{CO}(\text{O})\text{R}^4$, and $-\text{CO}(\text{O})\text{R}^5$, wherein any two R^{11} , R^{12} or R^{13} groups can optionally join to form a 3 to 8 membered cycloalkyl, aryl, heterocyclyl or heteroaryl ring, wherein the heterocyclyl or heteroaryl ring may contain one to three heteroatoms selected from $-\text{NR}^5$, $-\text{O}-$, $-\text{S}-$,

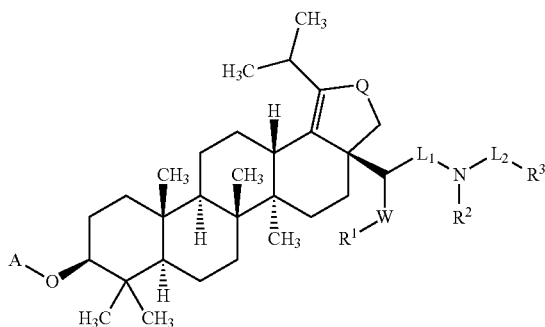
25

—S(O)—, or —SO₂—, and wherein the cycloalkyl, aryl, heterocyclyl or heteroaryl ring may be optionally substituted by one to three R¹⁶ groups;

R¹⁴ and R¹⁵ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, (C₁-C₆)alkoxy, —[C(R⁶)₂]_r—, —O[C(R⁶)₂]_r—, Oxo, hydroxyl, halo, —C(O)R⁷, —R¹⁰, and —CO(O)R², wherein R¹⁴ and R¹⁵ can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring or 4 to 8 membered heterocyclyl ring containing one to three heteroatoms selected from —NR⁵—, —O—, —S—, —S(O)—, or —SO₂—, wherein the cycloalkyl ring or heterocyclyl ring may be optionally substituted by one to three R¹⁶ groups;

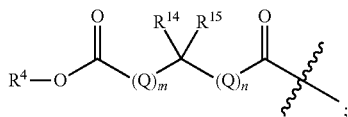
R¹⁶ is independently selected from the group consisting of —H, halo, oxo, hydroxyl, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₃-C₈)cycloalkyl, —R⁶(R⁹)_q, —OR⁶(R⁹)_q, —N(R⁴)₂, —(CH₂)_r-heterocycle, —C(O)OH, —C(O)NH₂, —R⁵(R⁹)_q, —OR⁵(R⁹)_q, nitro, —SO₂R⁶, —C(O)R¹⁰, and —CO(O)R⁴; m and n in each instance are independently 0, 1, 2, 3, or 4; p is independently 0, 1, 2, 3, or 4; r and q in each instance are independently 0, 1, 2, 3, or 4.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula II:



or a pharmaceutically acceptable salt thereof, wherein:

A is

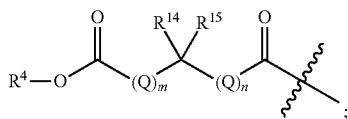


L₁ and L₂ are [C(R⁶R^{6a})_q];

each Q is independently selected from —CH₂— or —C(=O)—;

W is selected from a bond or O;

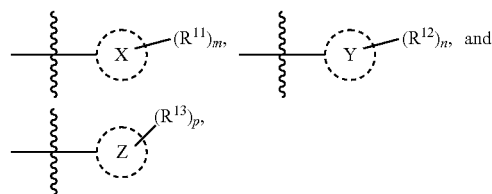
R¹ is selected from the group consisting of —H, (C₁-C₆)alkyl, —C(O)R⁴, and



R² is selected from the group consisting of —H, (C₁-C₆)alkyl, —(C₁-C₆)alkyl-OR⁴, —(C₁-C₆)alkyl-O—(C₁-C₆)alkyl, —C(O)R⁵, —(CH₂)_rNR⁷R⁸, and —(CH₂)_rN⁺(R⁴)₃;

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R³ is selected from the group consisting of —H, (C₁-C₁₂)alkyl, —NR¹R², —OR⁵,



wherein:

X is a monocyclic or bicyclic (C₅-C₁₄)aryl,

Y is selected from a monocyclic or bicyclic (C₂-C₉)heterocyclyl or monocyclic or bicyclic (C₂-C₉)heteroaryl, each having one to three heteroatoms selected from S, N or O, and

Z is a monocyclic or bicyclic (C₃-C₈)cycloalkyl;

R⁴ is selected from the group consisting of —H and (C₁-C₆)alkyl;

R⁵ is selected from the group consisting of (C₁-C₆)alkyl, —(CH₂)_rNR⁷R⁸, and —(CH₂)_rOR⁷;

R⁶ and R^{6a} are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, (C₁-C₆)alkoxy, haloalkyl, —(CH₂)_rNR⁷R⁸, —C(O)OH, and —C(O)NH₂, wherein the R⁶ and R^{6a} groups can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring, and wherein the cycloalkyl ring may be optionally substituted by one to three R¹¹ groups;

R⁷ and R⁸ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, —NR¹⁴R¹⁵, and —C(O)CH₃;

R⁹ is halo;

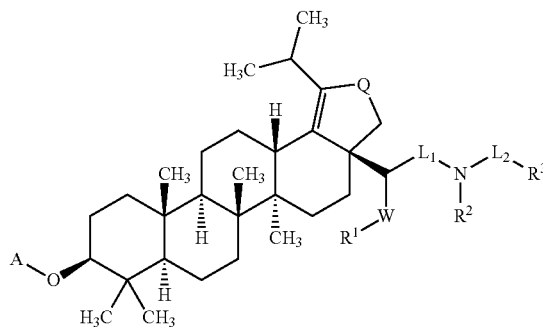
R¹⁰ is —N(R¹⁶)₂;

R¹¹, R¹², and R¹³ are independently selected from the group consisting of oxo, hydroxyl, halo, (C₁-C₆)alkoxy, —R⁶(R⁹)_q, —OR⁶(R⁹)_q, nitro, —SO₂R⁶, (C₁-C₆)alkyl, —C(O)R¹⁰, —R⁴YR⁶, —CO(O)R⁴, and —CO(O)R²;

R¹⁴ and R¹⁵ are independently selected from the group consisting of —H, (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, (C₁-C₆)alkoxy, —[C(R⁶)₂]_r—, —O[C(R⁶)₂]_r—, oxo, hydroxyl, halo, —C(O)R⁷, —R¹⁰, and —CO(O)R²;

R¹⁶ is independently selected from the group consisting of —H, oxo, halo, hydroxyl, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₃-C₈)cycloalkyl, —R⁶(R⁹)_q, —OR⁶(R⁹)_q, —N(R⁴)₂, —(CH₂)_r-heterocycle, —C(O)OH, —C(O)NH₂, —R⁵(R⁹)_q, —OR⁵(R⁹)_q, nitro, —SO₂R⁶, —C(O)R¹⁰, and —CO(O)R⁴; m and n in each instance are independently 0, 1, 2, 3, or 4; p is independently 0, 1, 2, 3, or 4; r and q in each instance are independently 0, 1, 2, 3, or 4.

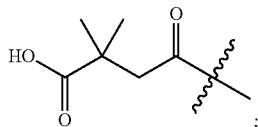
In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula II:



27

or a pharmaceutically acceptable salt thereof, wherein:

A is



L_1 and L_2 are both $(-\text{CH}_2-)$;

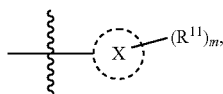
Q is $-\text{C}(=\text{O})-$;

W is O;

R^1 is $-\text{H}$;

R^2 is selected from the group consisting of $-\text{H}$, $(\text{C}_1\text{-C}_6)$ alkyl, $-\text{C}(\text{O})\text{R}^5$, and $-(\text{CH}_2)_r\text{NR}^7\text{R}^8$;

R^3 is



wherein X is a monocyclic or bicyclic $(\text{C}_5\text{-C}_{14})$ aryl;

R^4 is selected from the group consisting of $-\text{H}$ and $(\text{C}_1\text{-C}_6)$ alkyl;

R^5 is selected from the group consisting of $(\text{C}_1\text{-C}_6)$ alkyl, $-(\text{CH}_2)_r\text{NR}^7\text{R}^8$, and $-(\text{CH}_2)_r\text{OR}^7$;

R^6 is selected from the group consisting of $-\text{H}$, $(\text{C}_1\text{-C}_6)$ alkyl, $(\text{C}_3\text{-C}_8)$ cycloalkyl, $(\text{C}_1\text{-C}_6)$ alkoxy, haloalkyl, $-(\text{CH}_2)_r\text{NR}^7\text{R}^8$, $-\text{C}(\text{O})\text{OH}$, and $-\text{C}(\text{O})\text{NH}_2$;

R^7 and R^8 are independently selected from the group consisting of $-\text{H}$, $(\text{C}_1\text{-C}_6)$ alkyl, $(\text{C}_3\text{-C}_8)$ cycloalkyl, $-\text{NR}^{14}\text{R}^{15}$, and $-\text{C}(\text{O})\text{CH}_3$;

R^9 is halo;

R^{10} is $-\text{N}(\text{R}^{16})_2$;

R^{11} , R^{12} , and R^{13} are independently selected from the group consisting of oxo, hydroxyl, halo, $(\text{C}_1\text{-C}_6)$ alkoxy, $-\text{R}^6(\text{R}^9)_q$, $-\text{OR}^6(\text{R}^9)_q$, nitro, $-\text{SO}_2\text{R}^6$, $(\text{C}_1\text{-C}_6)$ alkyl, $-\text{C}(\text{O})\text{R}^{10}$, $-\text{CO}(\text{O})\text{R}^4$, and $-\text{CO}(\text{O})\text{R}^5$;

R^{14} and R^{15} are independently selected from the group consisting of $-\text{H}$, $(\text{C}_1\text{-C}_6)$ alkyl, $(\text{C}_3\text{-C}_8)$ cycloalkyl, $(\text{C}_1\text{-C}_6)$ alkoxy, $-\text{C}(\text{O})\text{R}^7$, $-\text{R}^{16}$, and $-\text{CO}(\text{O})\text{R}^2$;

R^{16} is independently selected from the group consisting of $-\text{H}$, oxo, halo, hydroxyl, $(\text{C}_1\text{-C}_6)$ alkyl, $(\text{C}_1\text{-C}_6)$ alkoxy, $(\text{C}_3\text{-C}_8)$ cycloalkyl, $-\text{R}^6(\text{R}^9)_q$, $-\text{OR}^6(\text{R}^9)_q$, $-\text{N}(\text{R}^4)_2$, $-(\text{CH}_2)_r$ -heterocycle, $-\text{C}(\text{O})\text{OH}$, $-\text{C}(\text{O})\text{NH}_2$, $-\text{R}^5(\text{R}^9)_q$, $-\text{OR}^5(\text{R}^9)_q$, nitro, $-\text{SO}_2\text{R}^6$, $-\text{C}(\text{O})\text{R}^{10}$, and $-\text{CO}(\text{O})\text{R}^4$;

m and n in each instance are independently 0, 1, or 2;

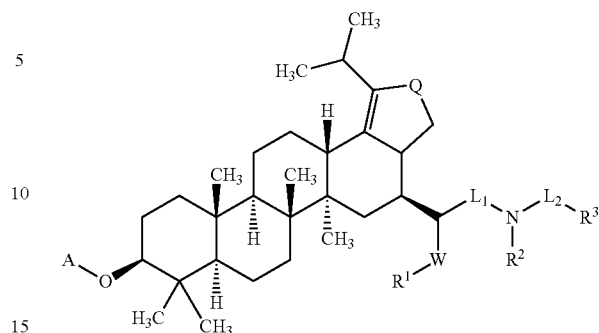
p is independently 0, 1, or 2; and

r and q in each instance are independently 0, 1, 2, or 3.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula II:

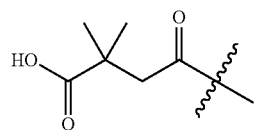
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(II)



or a pharmaceutically acceptable salt thereof, wherein:

A is



L_1 and L_2 are both $(-\text{CH}_2-)$;

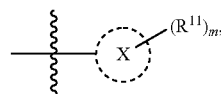
Q is $-\text{C}(=\text{O})-$;

W is O;

R^1 is $-\text{H}$;

R^2 is $-(\text{CH}_2)_r\text{NR}^7\text{R}^8$;

R^3 is



wherein X is phenyl;

R^7 and R^8 are independently selected from the group consisting of $-\text{H}$ and methyl;

R^9 is selected from the group consisting of chloro, bromo, and fluoro;

R^{11} is selected from the group consisting of chloro, bromo, and fluoro;

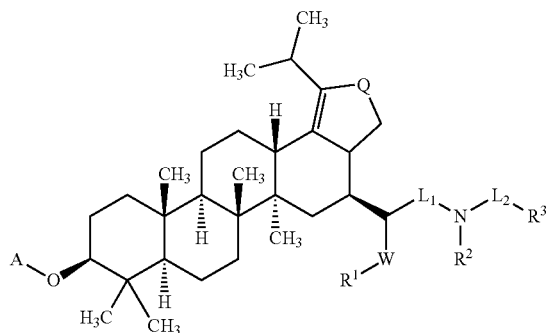
m is 0, 1, or 2; and

r is 1, 2, or 3.

In accordance with another embodiment of the present invention, there is provided a compound of Formula II:

Formula II

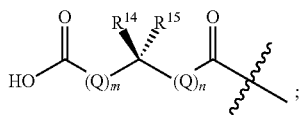
(II)



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or a pharmaceutically acceptable salt thereof, wherein:

A is

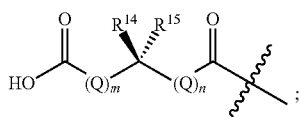


L_1 and L_2 are independently selected from a bond or $[C(R^6R^6)]_q$;

Q is selected from $-\text{CH}_2-$ or $-\text{C}(=\text{O})-$;

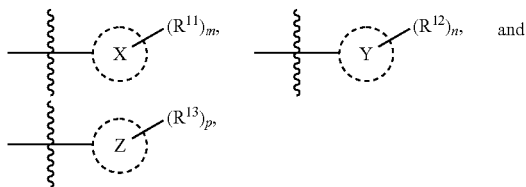
W is selected from a bond or oxygen;

R^1 is selected from the group consisting of $-\text{H}$, $(\text{C}_1-\text{C}_{12})$ alkyl, $-\text{C}(\text{O})\text{R}^5$, $-\text{CH}_2-\text{O}-(\text{C}_1-\text{C}_6)$ alkyl, 2-tetrahydro-2H-pyran and



R^2 is selected from the group consisting of $-\text{H}$, $(\text{C}_1-\text{C}_{12})$ alkyl, $-\text{C}_{1-6}$ alkyl-OH, $-\text{C}_{1-6}$ alkyl-O- C_{1-6} alkyl, $-\text{C}(\text{O})\text{R}^5$, and $-(\text{CH}_2)_n\text{NR}^7\text{R}^8$, $-\text{C}(\text{O})\text{R}^5$, wherein when W is oxygen, R^1 and R^2 can optionally be taken together with the oxygen and nitrogen to which they are respectively joined to form a 4 to 8 membered heterocyclyl ring, wherein the heterocyclyl ring may be optionally substituted by one to two R^{11} groups;

R^3 is selected from the group consisting of hydrogen, $(\text{C}_1-\text{C}_{12})$ alkyl, $-\text{NR}^7\text{R}^2$, $-\text{OR}^5$,



wherein:

X is a monocyclic or bicyclic $(\text{C}_5-\text{C}_{14})$ aryl,

Y is selected from a monocyclic or bicyclic (C_2-C_9) heterocyclyl or monocyclic or bicyclic (C_2-C_9) heteroaryl, each having one to three heteroatoms selected from S, N or O, and

Z is a monocyclic or bicyclic (C_3-C_8) cycloalkyl;

R^2 and R^3 can optionally be taken together with the nitrogen and L_2 to which they are respectively joined to form a 4 to 8 membered heterocyclyl ring, wherein the heterocyclyl ring may be optionally substituted by one to two R^{11} groups;

R^4 is selected from $-\text{H}$ and (C_1-C_6) alkyl;

R^5 is selected from (C_1-C_6) alkyl, $-\text{R}^3$, $-(\text{CH}_2)_n\text{NR}^7\text{R}^8$, or $-(\text{CH}_2)_n\text{OR}^7$;

R^6 and $R^{6'}$ are independently $-\text{H}$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, (C_1-C_6) alkoxy, haloalkyl, $-\text{Y}$, $-(\text{CH}_2)_n\text{NR}^7\text{R}^8$, $-\text{C}(\text{O})\text{OH}$, $-\text{C}(\text{O})\text{NH}_2$, wherein the R^6 and $R^{6'}$ groups can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring, wherein the cycloalkyl ring may be optionally substituted by one to three R^{11} groups;

R^7 and R^8 are independently selected from the group consisting of $-\text{H}$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, $-\text{Q-aryl}$ $(\text{R}^4)_m$, $-\text{NR}^{14}\text{R}^{15}$, $-\text{C}(\text{O})\text{CH}_3$, wherein R^7 and R^8 can optionally be taken together with the nitrogen to which they

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are joined to form a 4 to 8 membered heterocyclyl or heteroaryl ring containing one to three heteroatoms selected from $-\text{NR}^5$, $-\text{O}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, or $-\text{SO}_2-$, wherein the heterocyclyl or heteroaryl ring may be optionally substituted by one to three R^{11} groups;

R^9 is halo;

R^{10} is $-\text{N}(\text{R}^{16})_2$;

R^{11} , R^{12} , and R^{13} are independently selected from the group consisting of oxo, hydroxyl, halo, (C_1-C_6) alkoxy, $-\text{R}^6$ $(\text{R}^9)_q$, $-\text{OR}^6(\text{R}^9)_q$, nitro, $-\text{SO}_2\text{R}^6$, (C_1-C_6) alkyl, $-\text{C}(\text{O})\text{R}^{10}$, $-\text{R}^4\text{YR}^6$, and $-\text{CO}(\text{O})\text{R}^5$, wherein any two R^9 , R^{10} or R^{11} groups can optionally join to form a 3 to 8 membered cycloalkyl, aryl, heterocyclyl or heteroaryl ring, wherein the heterocyclyl or heteroaryl ring may contain one to three heteroatoms selected from $-\text{NR}^5$, $-\text{O}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, or $-\text{SO}_2-$, and wherein the cycloalkyl, aryl, heterocyclyl or heteroaryl ring may be optionally substituted by one to three R^{16} groups;

R^{14} and R^{15} are independently selected from the group consisting of $-\text{H}$, (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, (C_1-C_6) alkoxy, $-\text{C}(\text{R}^6)_2$, $-\text{O}[\text{C}(\text{R}^6)_2]_r$, oxo, hydroxyl, halo, $-\text{C}(\text{O})\text{R}^7$, $-\text{R}^{10}$, and $-\text{CO}(\text{O})\text{R}^2$, wherein R^{14} and R^{15} can optionally be taken together with the carbon to which they are joined to form a 3 to 8 membered cycloalkyl ring or 4 to 8 membered heterocyclyl ring containing one to three heteroatoms selected from $-\text{NR}^5$, $-\text{O}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, or $-\text{SO}_2-$, wherein the cycloalkyl ring or heterocyclyl ring may be optionally substituted by one to three R^{16} groups;

R^{16} is independently selected from the group consisting of halo, oxo, hydroxyl, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_3-C_8) cycloalkyl, $-\text{R}^6(\text{R}^9)_q$, $-\text{OR}^6(\text{R}^9)_q$, $-\text{N}(\text{R}^4)_2$, $-(\text{CH}_2)_n$, heterocyclyl, $-\text{C}(\text{O})\text{OH}$, $-\text{C}(\text{O})\text{NH}_2$, $-\text{R}^5(\text{R}^9)_q$, $-\text{OR}^5$ $(\text{R}^9)_q$, nitro, $-\text{SO}_2\text{R}^6$, $-\text{C}(\text{O})\text{R}^{10}$, and $-\text{CO}(\text{O})\text{R}^4$;

m and n in each instance are independently 0, 1, 2, 3, or 4;

p is independently 0, 1, 2, 3, or 4; and

r and q in each instance are independently 0, 1, 2, 3, or 4.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein L_1 and L_2 are both $[\text{C}(\text{R}^6\text{R}^{6'})]_q$.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above,

wherein L_1 and L_2 are both $-\text{CH}_2-$.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein q is independently 1, 2, or 3.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein q is 1.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein W is O.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein W is a bond.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein when W is a bond, then R^1 is $-\text{H}$.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein when W is O, then R^1 is $-\text{H}$.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein Q_m in the A group is absent and Q_n in the A group is $-\text{CH}_2-$ and the Q in the Formula I structure is $-\text{C}(=\text{O})-$.

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In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^1 is —H.

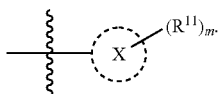
In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^2 is $-(CH_2)_rNR^7R^8$.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^2 is (dimethylamino)ethyl.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein r is independently 0, 1, 2, or 3.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein r is 2.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^3 is



In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein X is a monocyclic (C_5-C_{14})aryl.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein X is phenyl.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^4 is —H.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein m is 0 or 1.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein m is 0.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein m is 1.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein n is 1.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^6 and R^{6a} are both —H.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^7 and R^8 are both (C_1-C_6)alkyl.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^7 is methyl.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^8 is methyl.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^7 and R^8 are both methyl.

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In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^{11} is halo.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^{11} is selected from chloro, bromo, or fluoro.

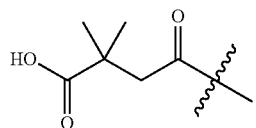
In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^{11} is chloro.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^{11} is absent.

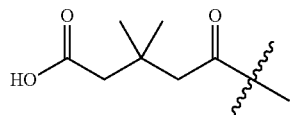
In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^{14} and R^{15} are both (C_1-C_6)alkyl.

In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein R^{14} and R^{15} are both methyl.

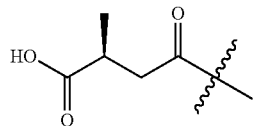
In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein A is



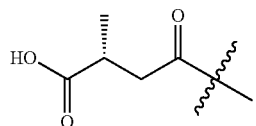
In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein A is



In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein A is

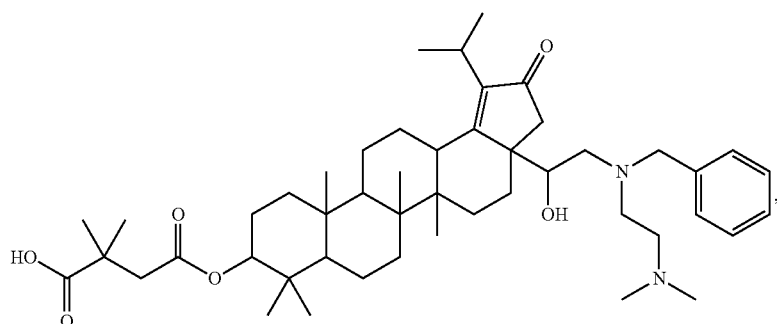


In accordance with another embodiment of the present invention, there is provided a compound having the structure of Formula I or Formula II above, wherein A is



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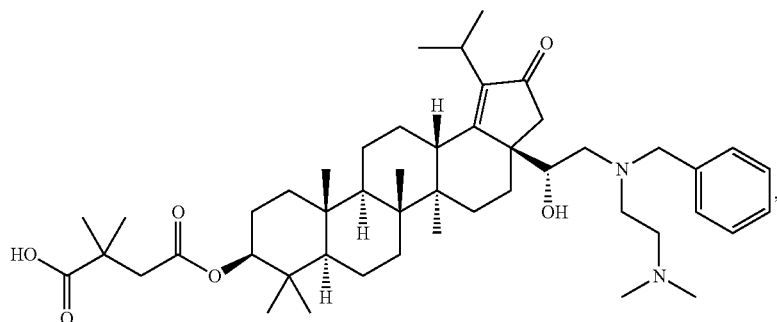
In accordance with another embodiment of the present invention, there is provided a compound having the structure:



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or a pharmaceutically acceptable salt thereof.

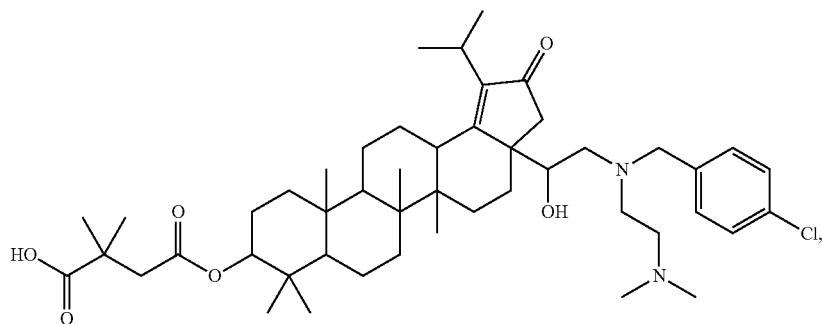
In accordance with another embodiment of the present invention, there is provided a compound having the structure:



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or a pharmaceutically acceptable salt thereof.

In accordance with another embodiment of the present invention, there is provided a compound having the structure:

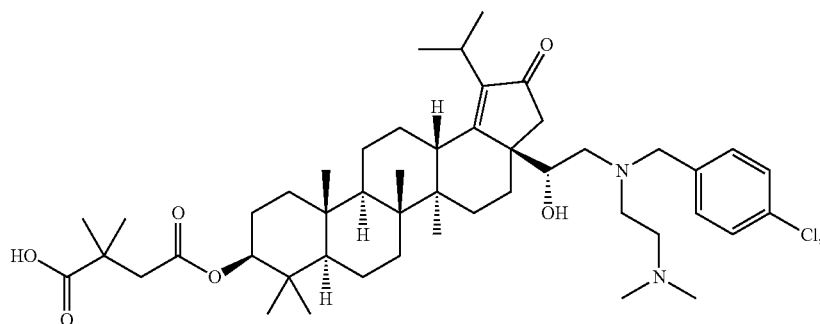


65

or a pharmaceutically acceptable salt thereof.

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In accordance with another embodiment of the present invention, there is provided a compound having the structure:



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at risk for developing an HIV infection, comprising administering to the subject a pharmaceutical composition compris-

or a pharmaceutically acceptable salt thereof.

In a further embodiment of the present invention, there is provided a pharmaceutical composition comprising a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable excipient.

In a further embodiment of the present invention, there is provided a method of treating HIV comprising administering to a patient suffering therefrom an effective amount of a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof.

In a further embodiment of the present invention, there is provided a pharmaceutical composition comprising a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

In a further embodiment of the present invention, there is provided a pharmaceutical composition comprising a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient, wherein the compound is present in an amorphous form.

In a further embodiment of the present invention, there is provided a pharmaceutical composition comprising a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient, wherein the composition is in a tablet form.

In a further embodiment of the present invention, there is provided a pharmaceutical composition comprising a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient, wherein the compound is present as a spray dried dispersion.

In a further embodiment of the present invention, there is provided a method of treating an HIV infection in a subject comprising administering to the subject a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof. In certain embodiments, the subject is a mammal, and in other embodiments, the subject is a human.

In a further embodiment of the present invention, there is provided a method of treating an HIV infection in a subject comprising administering to the subject a pharmaceutical composition comprising a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

In a further embodiment of the present invention, there is provided a method of preventing an HIV infection in a subject at risk for developing an HIV infection, comprising administering to the subject a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof.

In a further embodiment of the present invention, there is provided a method of preventing an HIV infection in a subject

ing a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

In still other embodiments, the present invention also provides the use of a compound or salt as defined in any of Formula I or Formula II in the manufacture of a medicament for use in the treatment of an HIV infection in a human.

Furthermore, the compounds of the invention can exist in particular geometric or stereoisomeric forms. The invention contemplates all such compounds, including cis- and trans-isomers, (-)- and (+)-enantiomers, (R)- and (S)-enantiomers, diastereomers, (D)-isomers, (L)-isomers, the racemic mixtures thereof, and other mixtures thereof, such as enantiomerically or diastereomerically enriched mixtures, as falling within the scope of the invention. Additional asymmetric carbon atoms can be present in a substituent such as an alkyl group. All such isomers, as well as mixtures thereof, are intended to be included in this invention.

Optically active (R)- and (S)-isomers and d and l isomers can be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. If, for instance, a particular enantiomer of a compound of the present invention is desired, it can be prepared by asymmetric synthesis, or by derivatization with a chiral auxiliary, where the resulting diastereomeric mixture is separated and the auxiliary group cleaved to provide the pure desired enantiomers. Alternatively, where the molecule contains a basic functional group, such as an amino group, or an acidic functional group, such as a carboxyl group, diastereomeric salts can be formed with an appropriate optically active acid or base, followed by resolution of the diastereomers thus formed by fractional crystallization or chromatographic means known in the art, and subsequent recovery of the pure enantiomers. In addition, separation of enantiomers and diastereomers is frequently accomplished using chromatography employing chiral, stationary phases, optionally in combination with chemical derivatization (e.g., formation of carbamates from amines).

In another embodiment of the invention, there is provided a compound of Formula I or Formula II, wherein the compound or salt of the compound is used in the manufacture of a medicament for use in the treatment of a viral infection in a human.

In another embodiment of the invention, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable diluent and a therapeutically effective amount of a compound as defined in Formula I.

In one embodiment, the pharmaceutical formulation containing a compound of Formula I or Formula II or a salt thereof is a formulation adapted for parenteral administration. In another embodiment, the formulation is a long-acting parenteral formulation. In a further embodiment, the formulation is a nano-particle formulation.

The compounds of the present invention and their salts, solvates, or other pharmaceutically acceptable derivatives thereof, may be employed alone or in combination with other therapeutic agents. Therefore, in other embodiments, the methods of treating and/or preventing an HIV infection in a subject may in addition to administration of a compound of Formula I or Formula II further comprise administration of one or more additional pharmaceutical agents active against HIV.

In such embodiments, the one or more additional agents active against HIV is selected from the group consisting of zidovudine, didanosine, lamivudine, zalcitabine, abacavir, stavudine, adefovir, adefovir dipivoxil, fozivudine, todoxil, emtricitabine, alovudine, amdoxovir, elvucitabine, nevirapine, delavirdine, efavirenz, loviride, immunocal, oltipraz, capravirine, lersivirine, GSK2248761, TMC-278, TMC-125, etravirine, saquinavir, ritonavir, indinavir, nelfinavir, amprenavir, fosamprenavir, brexanavir, darunavir, atazanavir, tipranavir, palinavir, lasinavir, enfuvirtide, T-20, T-1249, PRO-542, PRO-140, TNX-355, BMS-806, BMS-663068 and BMS-626529, 5-Helix, raltegravir, elvitegravir, GSK1349572, GSK1265744, vicriviroc (Sch-C), Sch-D, TAK779, maraviroc, TAK449, didanosine, tenofovir, lopinavir, and darunavir.

As such, the compounds of the present invention and any other pharmaceutically active agent(s) may be administered together or separately and, when administered separately, administration may occur simultaneously or sequentially, in any order. The amounts of the compounds of the present invention and the other pharmaceutically active agent(s) and the relative timings of administration will be selected in order to achieve the desired combined therapeutic effect. The administration in combination of a compound of the present invention and salts, solvates, or other pharmaceutically acceptable derivatives thereof with other treatment agents may be in combination by administration concomitantly in: (1) a unitary pharmaceutical composition including both compounds; or (2) separate pharmaceutical compositions each including one of the compounds. Alternatively, the combination may be administered separately in a sequential manner wherein one treatment agent is administered first and the other second or vice versa. Such sequential administration may be close in time or remote in time. The amounts of the compound(s) of Formula I or Formula II or salts thereof and the other pharmaceutically active agent(s) and the relative timings of administration will be selected in order to achieve the desired combined therapeutic effect.

In addition, the compounds of the present invention may be used in combination with one or more other agents useful in the prevention or treatment of HIV.

Examples of Such Agents Include

Nucleotide reverse transcriptase inhibitors such as zidovudine, didanosine, lamivudine, zalcitabine, abacavir, stavudine, adefovir, adefovir dipivoxil, fozivudine, todoxil, emtricitabine, alovudine, amdoxovir, elvucitabine, and similar agents;

Non-nucleotide reverse transcriptase inhibitors (including an agent having anti-oxidation activity such as immunocal, oltipraz, etc.) such as nevirapine, delavirdine, efavirenz, loviride, immunocal, oltipraz, capravirine, lersivirine, GSK2248761, TMC-278, TMC-125, etravirine, and similar agents;

Protease inhibitors such as saquinavir, ritonavir, indinavir, nelfinavir, amprenavir, fosamprenavir, brexanavir, darunavir, atazanavir, tipranavir, palinavir, lasinavir, and similar agents;

Entry, attachment and fusion inhibitors such as enfuvirtide (T-20), T-1249, PRO-542, PRO-140, TNX-355, BMS-806, BMS-663068 and BMS-626529, 5-Helix and similar agents;

Integrase inhibitors such as raltegravir, elvitegravir, GSK1349572, GSK1265744 and similar agents;

Maturation inhibitors such as PA-344 and PA-457, and similar agents; and

CXCR4 and/or CCR5 inhibitors such as vicriviroc (Sch-C), Sch-D, TAK779, maraviroc (UK 427,857), TAK449, as well as those disclosed in WO 02/74769, PCT/US03/39644, PCT/US03/39975, PCT/US03/39619, PCT/US03/39618, PCT/US03/39740, and PCT/US03/39732, and similar agents.

Further examples where the compounds of the present invention may be used in combination with one or more agents useful in the prevention or treatment of HIV are found in Table 1.

TABLE 1

FDA Approval	Brand Name	Generic Name	Manufacturer
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)			
1987	Retrovir	zidovudine, azidothymidine, AZT, ZDV	GlaxoSmithKline
1991	Videx	didanosine, dideoxyinosine, ddi	Bristol-Myers Squibb
1992	Hivid	zalcitabine, dideoxycytidine, ddC	Roche Pharmaceuticals
1994	Zerit	stavudine, d4T	Bristol-Myers Squibb
1995	Epivir	lamivudine, 3TC	GlaxoSmithKline
1997	Combivir	lamivudine + zidovudine	GlaxoSmithKline
1998	Ziagen	abacavir sulfate, ABC	GlaxoSmithKline
2000	Trizivir	abacavir + lamivudine + zidovudine	GlaxoSmithKline
2000	Videx EC	enteric coated didanosine, ddi EC	Bristol-Myers Squibb
2001	Viread	tenofovir disoproxil fumarate, TDF	Gilead Sciences
2003	Emtriva	emtricitabine, FTC	Gilead Sciences
2004	Epzicom	abacavir + lamivudine	GlaxoSmithKline
2004	Truvada	emtricitabine + tenofovir disoproxil fumarate	Gilead Sciences
Non-Nucleosides Reverse Transcriptase Inhibitors (NNRTIs)			
1996	Viramune	nevirapine, NVP	Boehringer Ingelheim
1997	Rescriptor	delavirdine, DLV	Pfizer
1998	Sustiva	efavirenz, EFV	Bristol-Myers Squibb
2008	Intelence	etravirine	Tibotec Therapeutics
Protease Inhibitors (PIs)			
1995	Invirase	saquinavir mesylate, SQV	Roche Pharmaceuticals
1996	Norvir	ritonavir, RTV	Abbott Laboratories
1996	Crixivan	indinavir, IDV	Merck
1997	Viracept	nelfinavir mesylate, NFV	Pfizer
1997	Fortovase	saquinavir (no longer marketed)	Roche Pharmaceuticals
1999	Agenerase	amprenavir, APV	GlaxoSmithKline
2000	Kaletra	lopinavir + ritonavir, LPV/RTV	Abbott Laboratories

TABLE 1-continued

FDA Approval	Brand Name	Generic Name	Manufacturer
2003	Reyataz	atazanavir sulfate, ATV	Bristol-Myers Squibb
2003	Lexiva	fosamprenavir calcium, FOS-APV	GlaxoSmithKline
2005	Aptivus	tripranavir, TPV	Boehringer Ingelheim
2006	Prezista	darunavir	Tibotec Therapeutics
Fusion Inhibitors			
2003	Fuzeon	Enfuvirtide, T-20	Roche Pharmaceuticals & Trimeris
Entry Inhibitors			
2007	Selzentry	maraviroc	Pfizer
Integrase Inhibitors			
2007	Isentress	raltegravir	Merck

The scope of combinations of compounds of this invention with HIV agents is not limited to those mentioned above, but includes in principle any combination with any pharmaceutical composition useful for the treatment of HIV. As noted, in such combinations the compounds of the present invention and other HIV agents may be administered separately or in conjunction. In addition, one agent may be prior to, concurrent to, or subsequent to the administration of other agent(s).

The present invention may be used in combination with one or more agents useful as pharmacological enhancers as well as with or without additional compounds for the prevention or treatment of HIV. Examples of such pharmacological enhancers (or pharmacokinetic boosters) include, but are not limited to, ritonavir, GS-9350, and SPI-452.

Ritonavir is 10-hydroxy-2-methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)-4-thiazolyl]-3,6-dioxo-8,11-bis(phenylmethyl)-2,4,7,12-tetraazamidecan-13-oic acid, 5-thiazolylmethyl ester, [5S-(5S*,8R*,10R*,11R*)] and is available from Abbott Laboratories of Abbott park, Ill., as Norvir. Ritonavir is an HIV protease inhibitor indicated with other antiretroviral agents for the treatment of HIV infection. Ritonavir also inhibits P450 mediated drug metabolism as well as the P-glycoprotein (Pgp) cell transport system, thereby resulting in increased concentrations of active compound within the organism.

GS-9350 is a compound being developed by Gilead Sciences of Foster City Calif. as a pharmacological enhancer.

SPI-452 is a compound being developed by Sequoia Pharmaceuticals of Gaithersburg, Md., as a pharmacological enhancer.

In one embodiment of the present invention, a compound of Formula I or Formula II is used in combination with ritonavir. In one embodiment, the combination is an oral fixed dose combination. In another embodiment, the compound of Formula I or Formula II is formulated as a long acting parenteral injection and ritonavir is formulated as an oral composition. In one embodiment, is a kit containing the compound of Formula I or Formula II formulated as a long acting parenteral injection and ritonavir formulated as an oral composition. In another embodiment, the compound of Formula I or Formula II is formulated as a long acting parenteral injection and ritonavir is formulated as an injectable composition. In one embodiment, is a kit containing the compound of Formula I or Formula II formulated as a long acting parenteral injection and ritonavir formulated as an injectable composition.

In another embodiment of the present invention, a compound of Formula I or Formula II is used in combination with GS-9350. In one embodiment, the combination is an oral fixed dose combination. In another embodiment, the compound of Formula I or Formula II is formulated as a long acting parenteral injection and GS-9350 is formulated as an oral composition. In one embodiment, there is provided a kit containing the compound of Formula I or Formula II formulated as a long acting parenteral injection and GS-9350 formulated as an oral composition. In another embodiment, the compound of Formula I or Formula II is formulated as a long acting parenteral injection and GS-9350 is formulated as an injectable composition. In one embodiment, is a kit containing the compound of Formula I or Formula II is formulated as a long acting parenteral injection and GS-9350 formulated as an injectable composition.

In one embodiment of the present invention, a compound of Formula I or Formula II is used in combination with SPI-452. In one embodiment, the combination is an oral fixed dose combination. In another embodiment, the compound of Formula I or Formula II is formulated as a long acting parenteral injection and SPI-452 is formulated as an oral composition. In one embodiment, there is provided a kit containing the compound of Formula I or Formula II formulated as a long acting parenteral injection and SPI-452 formulated as an oral composition. In another embodiment, the compound of Formula I or Formula II is formulated as a long acting parenteral injection and SPI-452 is formulated as an injectable composition. In one embodiment, there is provided a kit containing the compound of Formula I or Formula II formulated as a long acting parenteral injection and SPI-452 formulated as an injectable composition.

In one embodiment of the present invention, a compound of Formula I or Formula II is used in combination with compounds which are found in previously filed PCT/CN2011/0013021, which is herein incorporated by reference.

The above other therapeutic agents, when employed in combination with the chemical entities described herein, may be used, for example, in those amounts indicated in the Physicians' Desk Reference (PDR) or as otherwise determined by one of ordinary skill in the art.

In another embodiment of the invention, there is provided a method for treating a viral infection in a mammal mediated at least in part by a virus in the retrovirus family of viruses which method comprises administering to a mammal, that has been diagnosed with said viral infection or is at risk of developing said viral infection, a compound of Formula I or Formula II.

In another embodiment of the invention, there is provided a method for treating a viral infection in a mammal mediated at least in part by a virus in the retrovirus family of viruses which method comprises administering to a mammal, that has been diagnosed with said viral infection or is at risk of developing said viral infection, a compound of Formula I or Formula II, wherein said virus is an HIV virus. In some embodiments, the HIV virus is the HIV-1 virus.

In another embodiment of the invention, there is provided a method for treating a viral infection in a mammal mediated at least in part by a virus in the retrovirus family of viruses which method comprises administering to a mammal, that has been diagnosed with said viral infection or is at risk of developing said viral infection, a compound of Formula I or Formula II, further comprising administration of a therapeutically effective amount of one or more agents active against an HIV virus.

In another embodiment of the invention, there is provided a method for treating a viral infection in a mammal mediated at least in part by a virus in the retrovirus family of viruses which method comprises administering to a mammal, that has been diagnosed with said viral infection or is at risk of developing said viral infection, a compound of Formula I or Formula II, further comprising administration of a therapeutically effective amount of one or more agents active against an HIV virus.

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oping said viral infection, a compound of Formula I or Formula II, further comprising administration of a therapeutically effective amount of one or more agents active against the HIV virus, wherein said agent active against HIV virus is selected from Nucleotide reverse transcriptase inhibitors; Non-nucleotide reverse transcriptase inhibitors; Pro-

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tease inhibitors; Entry, attachment and fusion inhibitors; Integrase inhibitors; Maturation inhibitors; CXCR4 inhibitors; and CCR5 inhibitors.

In further embodiments, the compound of the present invention, or a pharmaceutically acceptable salt thereof, is chosen from the compounds set forth in Table 2.

TABLE 2

Ex- am- ple No.	Parent Structure	Chemical Name
1		4-[(1R)-1- [(1R,2R,5R,10S,13R,14R, 17S,19R)-17-[(3- carboxy-3,3- dimethylpropanoyl)oxy]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-5-yl]-2-[[4- chlorophenyl)methyl] amino]ethoxy]-2,2-dimethyl- 4-oxobutanoic acid
2		4-[(1R)-1- [(1R,2R,5R,10S,13R,14R, 17S,19R)-17-[(3- carboxy-3,3- dimethylpropanoyl)oxy]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-5-yl]-2-[[4- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino]ethoxy]-2,2-dimethyl- 4-oxobutanoic acid
3		4-[(1S)-1- [(1R,2R,5R,10S,13R,14R, 17S,19R)-17-[(3- carboxy-3,3- dimethylpropanoyl)oxy]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-5-yl]-2-[[4- chlorophenyl)methyl]amino] ethoxy]-2,2-dimethyl- 4-oxobutanoic acid

TABLE 2-continued

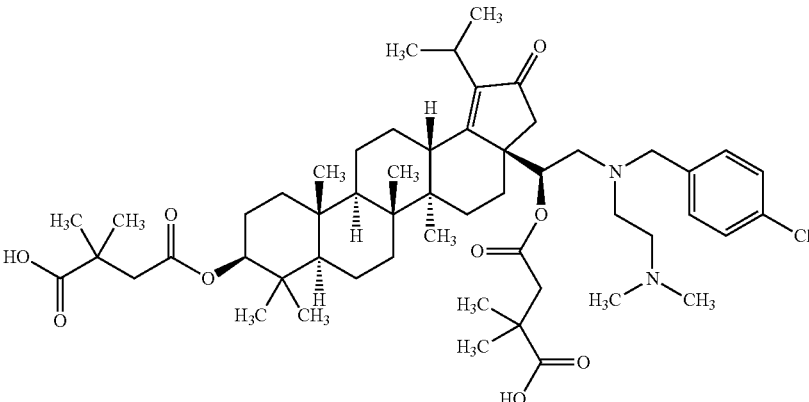
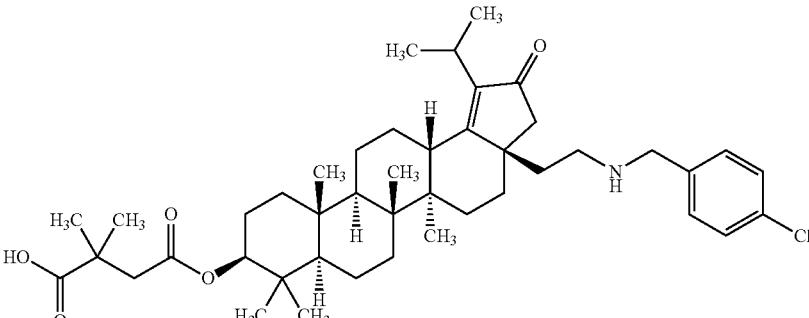
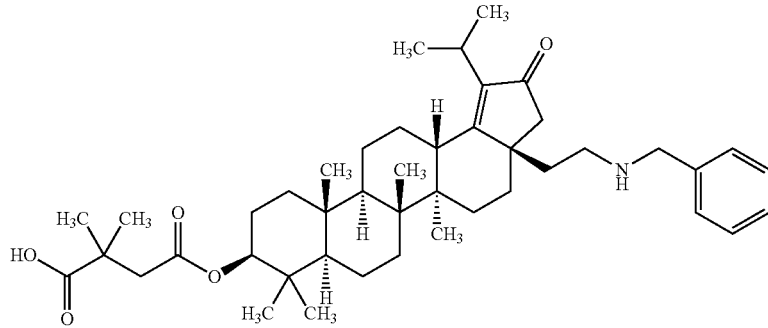
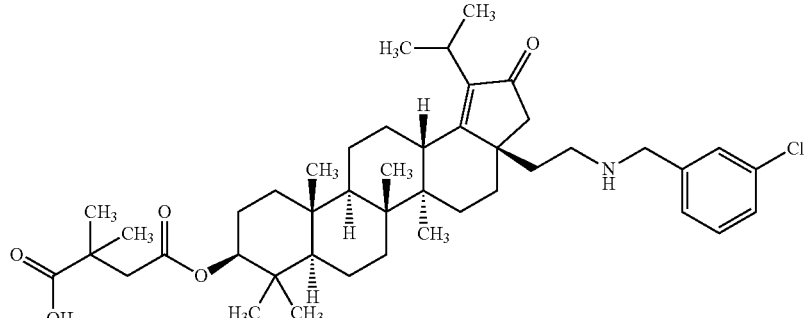
Ex- am- ple No.	Parent Structure	Chemical Name
4		4-[(1S)-1- [(1R,2R,5R,10S,13R,14R, 17S,19R)-17-[(3- carboxy-3,3- dimethylpropanoyl)oxy]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10].0 ^{5,9} .0 ^{14,19}] henicos-8-en-5-yl]-2-[[4- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino]ethoxy]-2,2-dimethyl- 4-oxobutanoic acid
5		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-[[4- chlorophenyl)methyl] amino]ethyl)-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10].0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
6		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[2- (benzylamino)ethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10].0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
7		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-[[3- chlorophenyl)methyl] amino]ethyl)-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10].0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
8		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-[[3- chloro-2- fluorophenyl)methyl] amino]ethyl)-1,2,14,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ .5,9 ¹⁰ .14,19 ¹⁷] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
9		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-[[1-(4- chlorophenyl)cyclopropyl] amino]ethyl)- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ .5,9 ¹⁰ .14,19 ¹⁷] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
10		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-[[4- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino]ethyl)-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ .5,9 ¹⁰ .14,19 ¹⁷] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
11		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-[[1-(4- chlorophenyl)cyclopropyl] [2- (dimethylamino)ethyl]amino] ethyl)-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ .5,9 ¹⁰ .14,19 ¹⁷] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
12		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-[[4- chlorophenyl)methyl] (methylamino)ethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}]] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
13		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-{N-[[4- chlorophenyl)methyl] acetamido}ethyl)- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}]] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
14		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(4- chlorophenyl)methyl]amino}- 1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}]] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
15		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(4- chlorophenyl)methyl]amino}- 1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}]] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
16		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(4- chlorophenyl)methyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
17		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-1- (acetyloxy)-2-[[4- chlorophenyl)methyl] amino]ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
18		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(4- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
19		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(4- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
20		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-1- (acetyloxy)-2-[[4- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino}ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ .5,9 ⁵ .0 ⁶ .14,19 ⁷] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
21		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-1- (acetyloxy)-2-[[4- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino}ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ .5,9 ⁵ .0 ⁶ .14,19 ⁷] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
22		5- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(4- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ .5,9 ⁵ .0 ⁶ .14,19 ⁷] henicos-8-en-17-yl]oxy}- 3,3-dimethyl-5- oxopentanoic acid
23		5- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(4- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ .5,9 ⁵ .0 ⁶ .14,19 ⁷] henicos-8-en-17-yl]oxy}- 3,3-dimethyl-5- oxopentanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
24		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(2- chlorophenyl)methyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ^ˆ {2, 10}.0 ^ˆ {5,9}.0 ^ˆ {14,19}} henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
25		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(2- chlorophenyl)methyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ^ˆ {2, 10}.0 ^ˆ {5,9}.0 ^ˆ {14,19}} henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
26		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-1- (acetyloxy)-2-[[4- fluorophenyl)methyl] amino}ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ^ˆ {2, 10}.0 ^ˆ {5,9}.0 ^ˆ {14,19}} henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
27		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-1- (acetyloxy)-2-[[4- fluorophenyl)methyl]amino} ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ^ˆ {2, 10}.0 ^ˆ {5,9}.0 ^ˆ {14,19}} henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
28		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((S)-1-acetoxy-2-((4- fluorobenzyl)(methyl) amino)ethyl)-1-isopropyl- 5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid
29		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(4- chlorophenyl)methyl] (methyl)amino}-1- hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0^2, 10].0^5,9.0^14,19}} heneicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
30		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((R)-1-Acetoxy-2-((4- chlorobenzyl)(methyl) amino)ethyl)-1-isopropyl- 5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
31		<p>4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(4- chlorophenyl)methyl] (methylamino)-1- hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0², 10³.0⁵{5,9}.0¹⁴{14,19}] henicos-8-en-17-yl]oxy]- 2,2-dimethyl-4- oxobutanoic acid</p>
32		<p>4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((S)-1-Acetoxy-2-(N-(4- chlorobenzyl)acetamido) ethyl)-1-isopropyl- 5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid</p>
32		<p>4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2-[N- [(4- chlorophenyl)methyl] acetamido]-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0², 10³.0⁵{5,9}.0¹⁴{14,19}] henicos-8-en-17-yl]oxy]- 2,2-dimethyl-4- oxobutanoic acid</p>

TABLE 2-continued

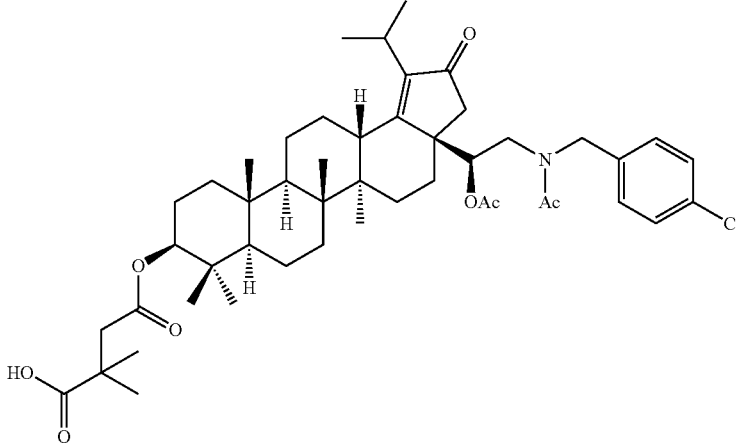
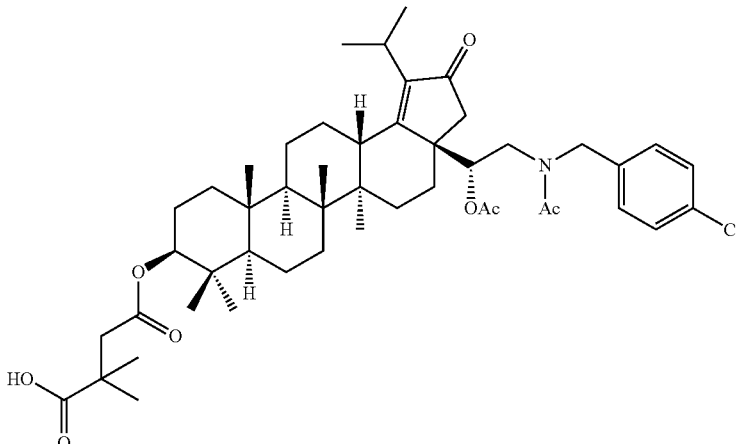
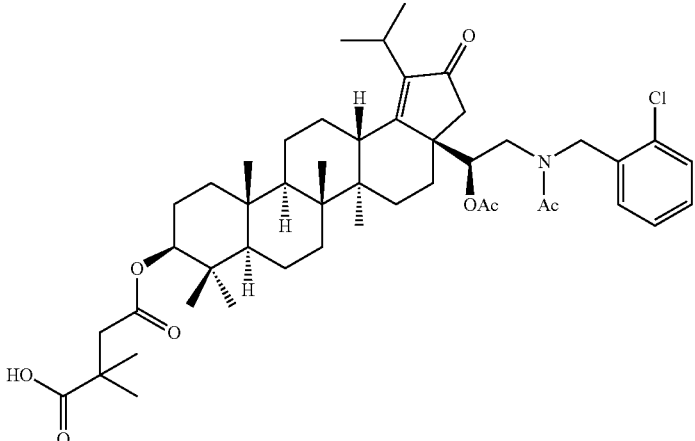
Ex- am- ple No.	Parent Structure	Chemical Name
33		4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(N-(4-Chlorobenzyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid
34		4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(N-(4-Chlorobenzyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid
35		4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(N-(2-Chlorobenzyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

TABLE 2-continued

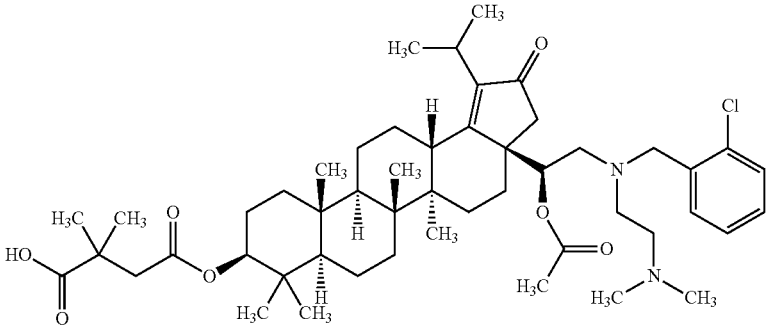
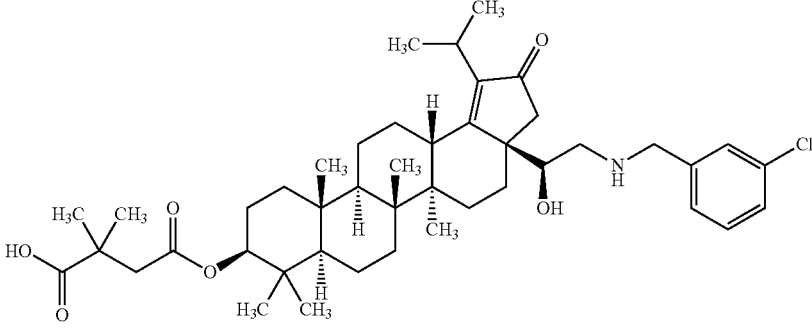
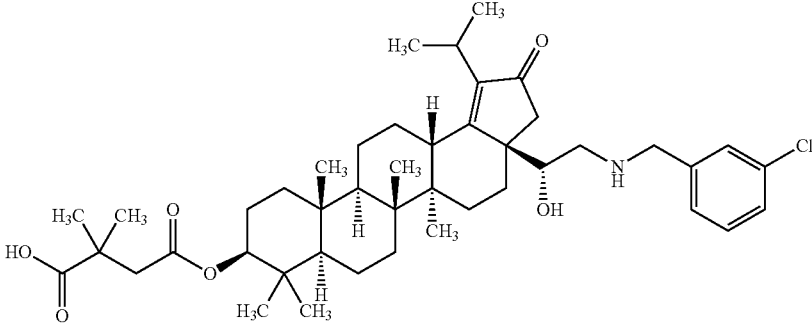
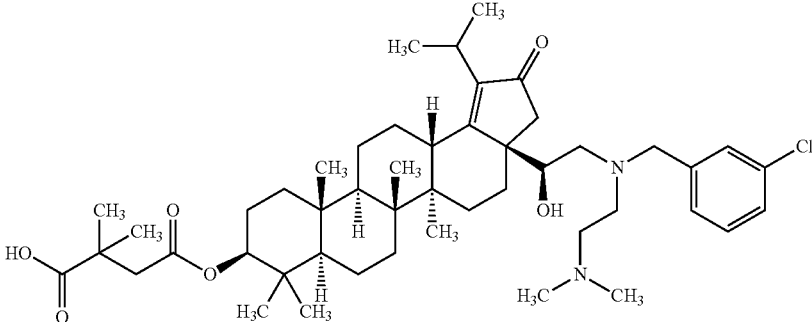
Ex- am- ple No.	Parent Structure	Chemical Name
36		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-1- (acetyloxy)-2-[[2- (dimethylamino)ethyl]amino] ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
37		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(3- chlorophenyl)methyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
38		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(3- chlorophenyl)methyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
37		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(3- chlorophenyl)methyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
38		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(3- chlorophenyl)methyl][2- (dimethylamino)ethyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ {5,9}.0 ⁵ {14,19}] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
39		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-1- (acetyloxy)-2-{[(3- chlorophenyl)methyl] amino}ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ {5,9}.0 ⁵ {14,19}] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
40		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-1- (acetyloxy)-2-{[(3- chlorophenyl)methyl] amino}ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ⁴ {5,9}.0 ⁵ {14,19}] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
41		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((S)-1-acetoxy-2-((3- chlorobenzyl)(2- (dimethylamino)ethyl) amino)ethyl)-1-isopropyl- 5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl]oxy)-2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

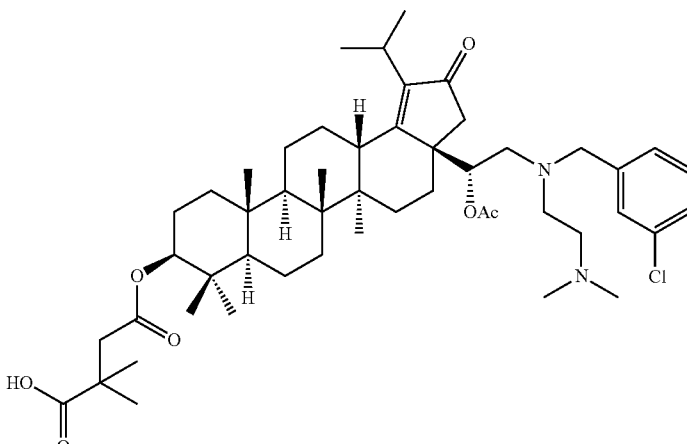
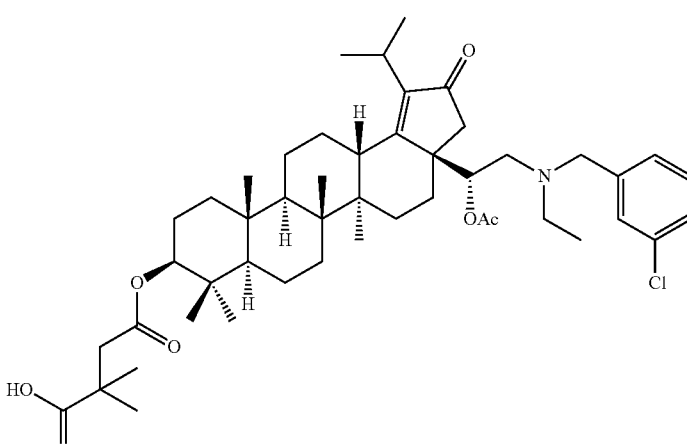
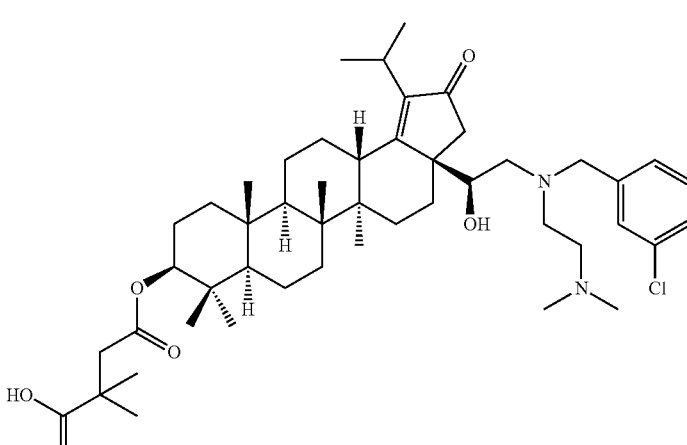
Ex- am- ple No.	Parent Structure	Chemical Name
42		4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-acetoxy-2-((3-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid
43		4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((3-chlorobenzyl)(ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid
44		4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((3-Chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
45		<p>4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)- 3a-((R)-2-((3- Chlorobenzyl)(2- (dimethylamino)ethyl) amino)-1-hydroxyethyl)- 1-isopropyl- 5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a, 8,9,10,11,11a,11b,12, 13,13a- octadecahydro-2H- cyclopenta[a]chrysen- 9-yl)oxy)-2,2-dimethyl- 4-oxobutanoic acid.</p>
46		<p>4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2-{N- [(3- chlorophenyl)methyl] acetamido}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0^{2,10}.0^{5,9}.0^{14,19}] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid</p>
47		<p>4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2-{N- [(3- chlorophenyl)methyl] acetamido}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0^{2,10}.0^{5,9}.0^{14,19}] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid</p>

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
48		4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-acetoxy-2-((2-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid
49		4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-chlorobenzyl)(ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid
50		4-{{{[(1R,2R,5R,10S,13R,14R,17S,19R)-5-[(1R)-2-{{{[2-chlorophenyl)methyl][2-(dimethylamino)ethyl]amino}-1-hydroxyethyl]-1,2,14,18,18-pentamethyl-7-oxo-8-(propan-2-yl)pentacyclo[11.8.0.0^{2,10}.0^{5,9}.0^{14,19}]}henicos-8-en-17-yl]oxy}-2,2-dimethyl-4-oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
51		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(2- chlorophenyl)methyl][2- (dimethylamino)ethyl]amino}- 1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
52		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-1- (acetyloxy)-2- (benzylamino)ethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
53		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-1- (acetyloxy)-2- (benzylamino)ethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
54		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((R)-2-((3-Chloro-2- fluorobenzyl)amino)-1- hydroxyethyl)-1- isopropyl-5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl]oxy)-2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

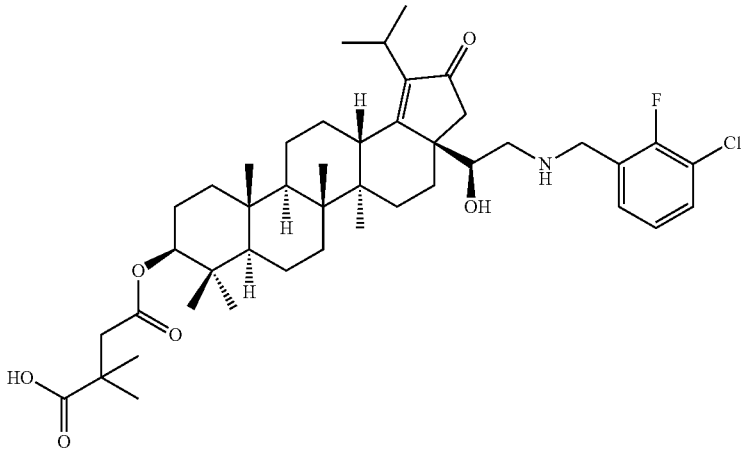
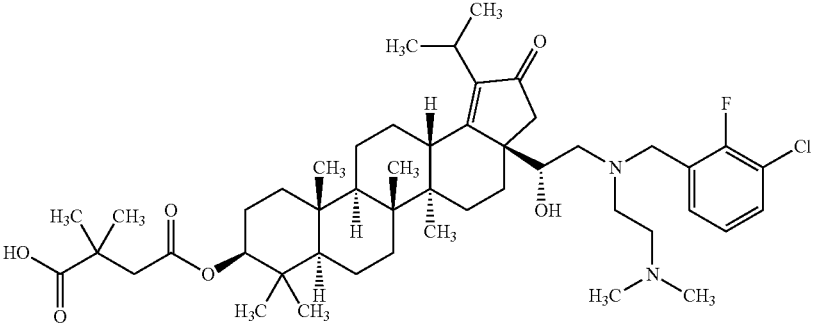
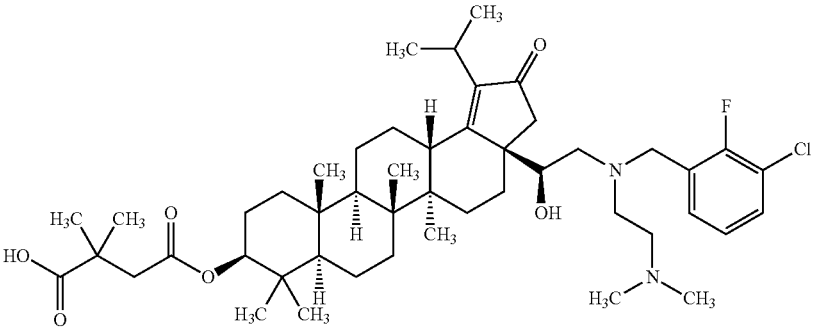
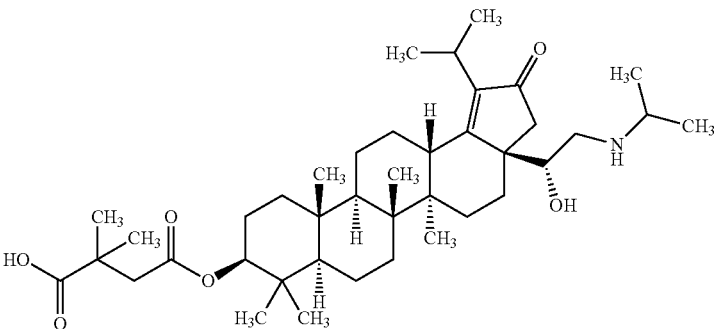
Ex- am- ple No.	Parent Structure	Chemical Name
55		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((S)-2-((3-chloro-2- fluorobenzyl)amino)-1- hydroxyethyl)-1- isopropyl-5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid
56		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(3-chloro-2- fluorophenyl)methyl][2- (dimethylamino)ethyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}]} henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
57		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(3-chloro-2- fluorophenyl)methyl][2- (dimethylamino)ethyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}]} henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
58		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-1- hydroxy-2-[(propan-2- yl)amino]ethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 10 ³ .0 ^{5,9} .0 ^{14,19}]} henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
59		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- (cyclohexylamino)-1- hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}]] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
53		4- {[(1R,2R,5S,10S,13R,14R, 17S,19R)-5-[1- hydroxy-2-(4- methylpiperazin-1- yl)ethyl]-1,2,14,18,18- pentamethyl-8-(propan- 2-yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}]] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
54		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-[[4- chlorophenyl)methyl] amino]ethyl)-1,2,14,18,18- pentamethyl-8-(propan- 2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}]] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
55		4- {[(1R,2R,5S,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(4- chlorophenyl)methyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-8-(propan- 2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}]] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
56		4- {[(1R,2R,5S,10S,13R,14R, 17S,19R)-5-[(1S)-2- [(cyclohexylmethyl) amino]-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-8-(propan- 2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} {5,9}.0 ^{14,19} }] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
57		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- (cyclohexylamino)-1- hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} {5,9}.0 ^{14,19} }] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
58		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-1- hydroxy-2-(1,2,3,4- tetrahydroisoquinolin-2- yl)ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} {5,9}.0 ^{14,19} }] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
59		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-1- hydroxy-2-(1,2,3,4- tetrahydroisoquinolin-2- yl)ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} {5,9}.0 ^{14,19} }] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
60		4- {[(1R,2R,10S,13R,14R,17S, 19R)-5-[(5S)-3-[1-(5- chloropyrimidin-2- yl)cyclopropyl]-2-oxo-1,3- oxazolidin-5-yl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ¹⁰].0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
61		4- {[(1R,12R,10S,13R,14R,17S, 19R)-5-[(5R)-3-[1-(5- chloropyrimidin-2- yl)cyclopropyl]-2-oxo-1,3- oxazolidin-5-yl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ¹⁰].0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
62		5- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(4- chlorophenyl)methyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ¹⁰].0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 3,3-dimethyl-5- oxopentanoic acid
63		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((R)-2-(3,4- dihydroisoquinolin-2(1H)- yl)-1-hydroxyethyl)-1- isopropyl-5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

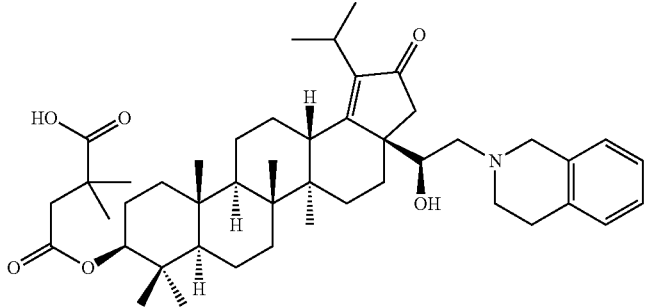
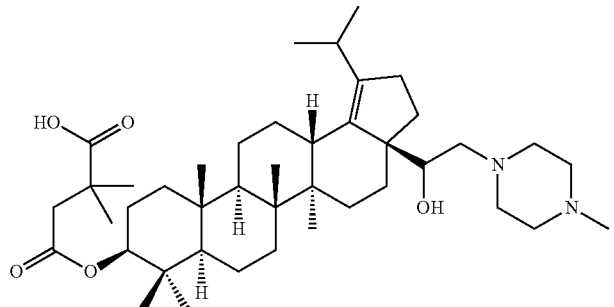
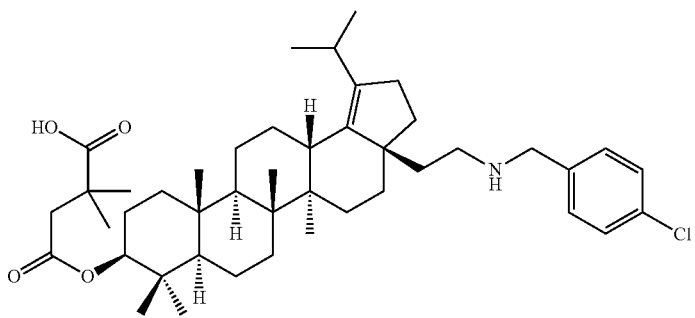
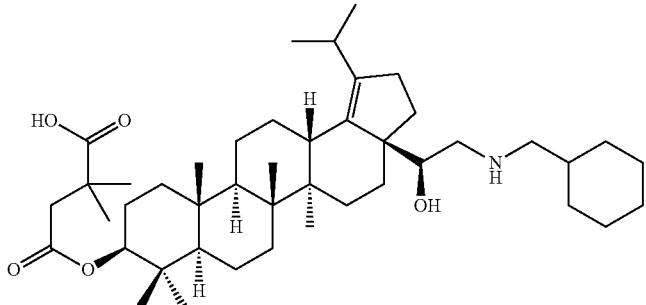
Ex- am- ple No.	Parent Structure	Chemical Name
64		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((S)-2-(3,4- dihydroisoquinolin-2(1H)- yl)-1-hydroxyethyl)-1- isopropyl-5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid
65		4- (((3aS,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((R)-1-hydroxy-2-(4- methylpiperazin-1- yl)ethyl)-1-isopropyl- 5a,5b,8,8,11a- pentamethyl- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid
66		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a-(2- ((4- chlorobenzyl)amino)ethyl)- 1-isopropyl- 5a,5b,8,8,11a- pentamethyl- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid
67		4- (((3aS,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((S)-2- ((cyclohexylmethyl)amino)- 1-hydroxyethyl)-1- isopropyl-5a,5b,8,8,11a- pentamethyl- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

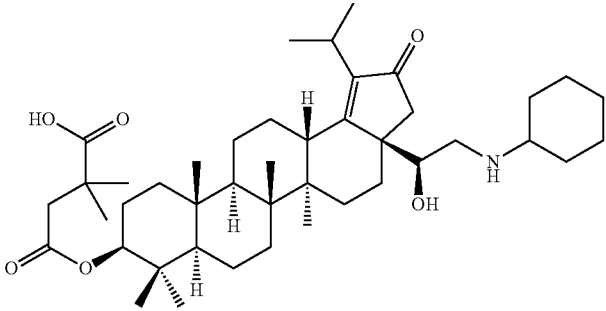
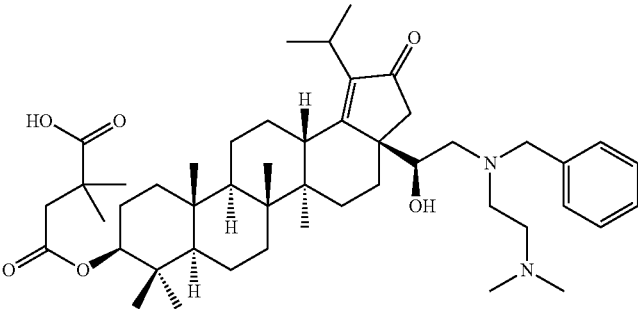
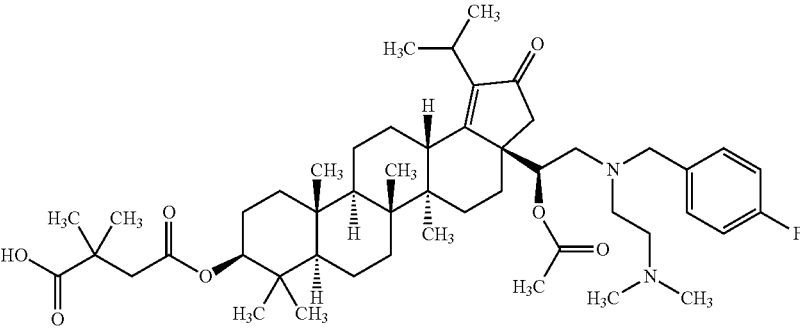
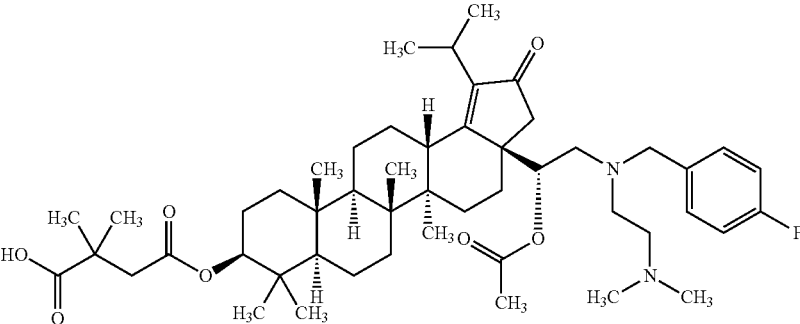
Ex- am- ple No.	Parent Structure	Chemical Name
68		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((S)-2-(cyclohexylamino)- 1-hydroxyethyl)-1- isopropyl-5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid
69		4- (((3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- ((S)-2-(benzyl(2- (dimethylamino)ethyl) amino)-1-hydroxyethyl)-1- isopropyl-5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl)oxy)-2,2-dimethyl-4- oxobutanoic acid
70		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-1- (acetyloxy)-2-{[2- (dimethylamino)ethyl][(4- fluorophenyl)methyl]amino} ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 2,10 ⁰ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid
71		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-1- (acetyloxy)-2-{[2- (dimethylamino)ethyl][(4- fluorophenyl)methyl]amino} ethyl]-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² . 2,10 ⁰ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy)- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
72		5- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(4- chlorophenyl)methyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 3,3-dimethyl-5- oxopentanoic acid
73		5- ([(3aR,5aR,5bR,7aR,9S, 11aR,11bR,13aS)-3a- (S)-2-((4- chlorobenzyl)amino)-1- hydroxyethyl)-1- isopropyl-5a,5b,8,8,11a- pentamethyl-2-oxo- 3,3a,4,5,5a,5b,6,7,7a,8,9, 10,11,11a,11b,12,13,13a- octadecahydro-2H- cyclopenta[a]chrysen-9- yl]oxy)-3,3-dimethyl-5- oxopentanoic acid
74		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(2,4- dichlorophenyl)methyl][2- (dimethylamino)ethyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
75		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {benzyl[2- (dimethylamino)ethyl] amino}-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² {2, 10}.0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
76		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[2- (dimethylamino)ethyl][(4- fluorophenyl)methyl]amino}- 1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
77		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1R)-2- {[(4- fluorophenyl)methyl]amino}- 1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
78		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[2- (dimethylamino)ethyl][(4- fluorophenyl)methyl]amino}- 1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
79		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[(1S)-2- {[(4- fluorophenyl)methyl]amino}- 1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ^{5,9} .0 ^{14,19}] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid

TABLE 2-continued

Ex- am- ple No.	Parent Structure	Chemical Name
80		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[[[(1R)-2- {[(2,4- dichlorophenyl)methyl][2- (dimethylamino)ethyl]amino}- 1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ⁵ ,9 ³ .0 ¹⁴ ,19 ³] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
81		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-[[[(1R)-2-[1- (4-chlorophenyl)-N-[2- (dimethylamino)ethyl] formamido]-1-hydroxyethyl]- 1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ⁵ ,9 ³ .0 ¹⁴ ,19 ³] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
82		4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)-5-(2-[[[(2- chlorophenyl)methyl]amino] ethyl)-1,2,14,18,18- pentamethyl-7-oxo-8- (propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ⁵ ,9 ³ .0 ¹⁴ ,19 ³] henicos-8-en-17-yl]oxy}- 2,2-dimethyl-4- oxobutanoic acid
83		2,2-dimethyl-4-oxo-4- {[(1R,2R,5R,10S,13R,14R, 17S,19R)- 1,2,14,18,18- pentamethyl-7-oxo-5-[2- (phenylformamido)ethyl]- 8-(propan-2- yl)pentacyclo[11.8.0.0 ² , 10 ³ .0 ⁵ ,9 ³ .0 ¹⁴ ,19 ³] henicos-8-en-17- yl]oxy}butanoic acid

The compounds of Table 2 were synthesized according to the Synthetic Methods, General Schemes, and the Examples described below.

In certain embodiments, the compound(s) of the present invention, or a pharmaceutically acceptable salt thereof, is chosen from the compounds set forth in Table 2.

Synthetic Methods

The methods of synthesis for the provided chemical entities employ readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or preferred process conditions (i.e., reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) are given; other process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures.

Additionally, the methods of this invention may employ protecting groups which prevent certain functional groups from undergoing undesired reactions. Suitable protecting groups for various functional groups as well as suitable conditions for protecting and deprotecting particular functional groups are well known in the art. For example, numerous protecting groups are described in T. W. Greene and G. M. Wuts, *Protecting Groups in Organic Synthesis*, Third Edition, Wiley, New York, 1999, and references cited therein.

Furthermore, the provided chemical entities may contain one or more chiral centers and such compounds can be prepared or isolated as pure stereoisomers, i.e., as individual enantiomers or diastereomers, or as stereoisomer-enriched mixtures. All such stereoisomers (and enriched mixtures) are included within the scope of this specification, unless otherwise indicated. Pure stereoisomers (or enriched mixtures) may be prepared using, for example, optically active starting materials or stereoselective reagents well-known in the art. Alternatively, racemic mixtures of such compounds can be separated using, for example, chiral column chromatography, chiral resolving agents and the like.

The starting materials for the following reactions are generally known compounds or can be prepared by known procedures or obvious modifications thereof. For example, many of the starting materials are available from commercial suppliers such as Aldrich Chemical Co. (Milwaukee, Wis., USA), Bachem (Torrance, Calif., USA), Ernc-Chemce or Sigma (St. Louis, Mo., USA). Others may be prepared by procedures, or obvious modifications thereof, described in standard reference texts such as Fieser and Fieser's *Reagents for Organic Synthesis*, Volumes 1-15 (John Wiley and Sons, 1991), *Rodd's Chemistry of Carbon Compounds*, Volumes 1-5 and *Supplementals* (Elsevier Science Publishers, 1989), *Organic Reactions*, Volumes 1-40 (John Wiley and Sons, 1991), *March's Advanced Organic Chemistry*, (John Wiley and Sons, 4th Edition), and *Larock's Comprehensive Organic Transformations* (VCH Publishers Inc., 1989).

Unless specified to the contrary, the reactions described herein take place at atmospheric pressure, generally within a temperature range from -78°C . to 200°C . Further, except as employed in the Examples or as otherwise specified, reaction times and conditions are intended to be approximate, e.g., taking place at about atmospheric pressure within a temperature range of about -78°C . to about 110°C . over a period of about 1 to about 24 hours; reactions left to run overnight average a period of about 16 hours.

The terms "solvent," "organic solvent," and "inert solvent" each mean a solvent inert under the conditions of the reaction being described in conjunction therewith, including, for example, benzene, toluene, acetonitrile, tetrahydrofuran (THF), dimethylformamide (DMF), chloroform, meth-

ylene chloride (or dichloromethane), diethyl ether, methanol, N-methylpyrrolidone ("NMP"), pyridine and the like.

Isolation and purification of the chemical entities and intermediates described herein can be effected, if desired, by any suitable separation or purification procedure such as, for example, filtration, extraction, crystallization, column chromatography, thin-layer chromatography or thick-layer chromatography, or a combination of these procedures. Specific illustrations of suitable separation and isolation procedures can be had by reference to the examples herein below. However, other equivalent separation or isolation procedures can also be used.

When desired, the (R)- and (S)-isomers may be resolved by methods known to those skilled in the art, for example by formation of diastereoisomeric salts or complexes which may be separated, for example, by crystallization; via formation of diastereoisomeric derivatives which may be separated, for example, by crystallization, gas-liquid or liquid chromatography; selective reaction of one enantiomer with an enantiomer-specific reagent, for example enzymatic oxidation or reduction, followed by separation of the modified and unmodified enantiomers; or gas-liquid or liquid chromatography in a chiral environment, for example on a chiral support, such as silica with a bound chiral ligand or in the presence of a chiral solvent. Alternatively, a specific enantiomer may be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents, or by converting one enantiomer to the other by asymmetric transformation.

EXAMPLES

The following examples serve to more fully describe the manner of making and using the above-described invention. It is understood that these examples in no way serve to limit the true scope of the invention, but rather are presented for illustrative purposes. In the examples below and the synthetic schemes above, the following abbreviations have the following meanings. If an abbreviation is not defined, it has its generally accepted meaning.

aq.=aqueous
 μL =microliters
 μM =micromolar
 NMR=nuclear magnetic resonance
 boc=tert-butoxycarbonyl
 br=broad
 Cbz=benzyloxycarbonyl
 d=doublet
 δ =chemical shift
 $^{\circ}\text{C}$ =degrees celcius
 DCM=dichloromethane
 dd=doublet of doublets
 DMEM=Dulbecco's Modified Eagle's Medium
 DMF=N,N-dimethylformamide
 DMSO=dimethylsulfoxide
 EtOAc=ethyl acetate
 g=gram
 h or hr=hours
 HCV=hepatitis C virus
 HPLC=high performance liquid chromatography
 Hz=hertz
 IU=International Units
 IC_{50} =inhibitory concentration at 50% inhibition
 J=coupling constant (given in Hz unless otherwise indicated)
 m=multiplet
 M=molar
 $\text{M}+\text{H}^{+}$ =parent mass spectrum peak plus H^{+}
 mg=milligram
 min=minutes
 mL=milliliter

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mM=millimolar
 mmol=millimole
 MS=mass spectrum
 nm=nanomolar
 ppm=parts per million
 q.s.=sufficient amount
 s=singlet
 RT=room temperature
 sat.=saturated
 t=triplet
 TFA=trifluoroacetic acid

Equipment Description

^1H NMR spectra were recorded on a Bruker Avance-III 400 spectrometer. Chemical shifts are expressed in parts per million (ppm, δ units). Coupling constants are in units of hertz (Hz). Splitting patterns describe apparent multiplicities and are designated as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), br (broad).

The analytical low-resolution mass spectra (MS) were recorded on Agilent 1200 HPLC/6110 or Agilent 1200 HPLC/6130 using a SunFire C18, 4.6 \times 50 mm, 3.5 μm using a gradient elution method.

Solvent A: 0.01% trifluoroacetic acid (TFA) in water;

Solvent B: 0.01% TFA in acetonitrile;

Constant A for 1.2 min followed by 5%-95% or 20%-95% B over 4 min.

Schemes and Experimental Procedures

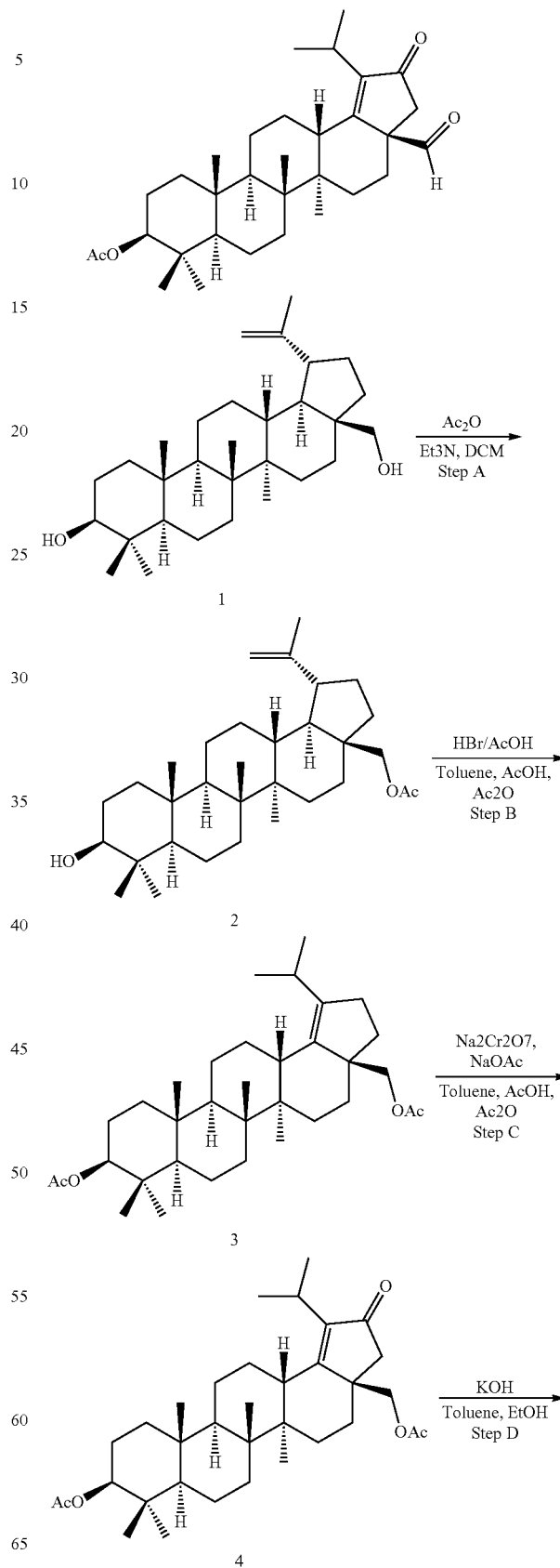
The following schemes and procedures illustrate how compounds of the present invention can be prepared. The specific solvents and reaction conditions referred to are also illustrative and are not intended to be limiting. Compounds not described are either commercially available or are readily prepared by one skilled in the art using available starting materials. The Examples disclosed herein are for illustrative purposes only and are not intended to limit the scope of the invention. All examples exhibited LHIV IC_{50} values between 1 μM and 1 nM using the assay disclosed herein.

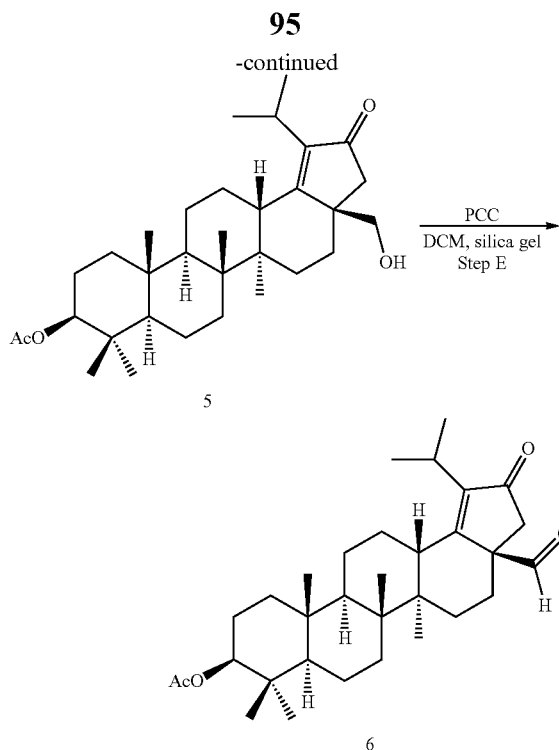
For several of the examples the stereochemistry of the C28 secondary alcohol when present was not definitively confirmed as to its absolute configuration. Unless stated otherwise, the compounds exemplified in the present application were isolated as optically pure stereoisomers and initially assigned to a configuration as drawn. There is the possibility that some of these may be listed as the opposite stereochemistry at that single C28 position as shown. This in no way is meant to limit the scope of the invention or utility of the compounds of Formula I. Additional examples contained within were determined to have the shown configuration by spectroscopic methods well known to those skilled in the art including, but not limited to, 1D and 2D NMR methods, vibrational circular dichroism and X-ray crystallography. These examples and the methods to make both diastereomers should serve to clearly exemplify the pure stereoisomers of both R and S configuration at the C28 position are readily obtained, separated and characterized and any remaining undefined examples could be readily confirmed by similar methods well known to one skilled in the art.

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Synthesis of aldehyde intermediate 6.

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Step A: Intermediate 2

((1R,3aS,5aR,5bR,7aR,9S,11aR,11bR,13aR,13bR)-9-Acetoxy-5a,5b, 8,8,11a-pentamethyl-1-(prop-1-en-2-yl)icosahydro-1H-cyclopenta[a]chrysen-3a-yl) methyl acetate

To a solution of the intermediate 1 (20 g, 45.2 mmol), 4-dimethylaminopyridine (DMAP, 1.66 g, 13.6 mmol), and Et₃N (63 mL, 136 mmol) in CH₂Cl₂ (DCM, 100 mL) at room temperature was added acetic anhydride (Ac₂O, 17.1 mL, 113 mmol). After it was heated at reflux overnight, and cooled down to room temperature, the reaction was quenched with water (50 mL). The organic phase was then washed with water (50 mL×2) and dried over sodium sulfate. After removing most of the organic solvent under reduced pressure, anhydrous ethanol (50 mL) was added and the resulting precipitates were collected by filtration as a white solid (intermediate 2, 20 g, 84%). ¹H NMR (400 MHz, CDCl₃) δ ppm 4.69 (1H, m), 4.59 (1H, m), 4.51-4.43 (1H, m), 4.25 (1H, d, J=11.2 Hz), 3.85 (1H, d, J=10.8 Hz), 2.49-2.40 (1H, m), 2.07 (3H, s), 2.04 (3H, s), 1.98-0.77 (42H, m). LC/MS: m/z calculated 526.4. found 527.7 (M+1)+.

Step B: Intermediate 3

((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-acetoxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)methyl acetate

HBr in acetic acid (40 mL, 33%) was added to a suspension of the intermediate 2 (20 g, 38 mmol) in toluene (40 mL), Ac₂O (40 mL), and acetic acid (AcOH, 40 mL) previously heated at 105° C. The reaction mixture was stirred and heated at this temperature for 1.5 h. After cooling down, sodium acetate (24 g) was added and the resulting reaction mixture was evaporated to dryness. The pale brownish residue was taken up in DCM (200 mL) and the organic phase was washed

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with water (100 mL×3), dried over sodium sulfate, and evaporated to dryness under reduced pressure to provide a residue, which was then recrystallized from ethanol (EtOH, 95%) and DCM, to afford the intermediate 3 (13.8 g, 69%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ ppm 4.50-4.46 (1H, m), 4.02 (1H, d, J=10.8 Hz), 3.98 (1H, d, J=10.8 Hz), 3.18-3.10 (1H, m), 2.43-2.40 (1H, m), 2.26-2.22 (2H, m), 2.04 (3H, s), 2.05 (3H, s), 2.00-1.95 (1H, m), 1.90-1.85 (1H, m), 1.77-0.83 (39H, m).

LC/MS: m/z calculated 526.4. found 549.2 (M+Na)+.

Step C: Intermediate 4

((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-Acetoxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl) methyl acetate

A mixture of the intermediate 3 (7 g, 13.29 mmol), sodium acetate (NaOAc, 6.21 g, 76 mmol) and sodium dichromate dihydrate (4.75 g, 15.95 mmol) in anhydrous toluene (90 mL), AcOH (119 mL), and Ac₂O (29 mL) was stirred at 60° C. overnight. After cooling down, the reaction mixture was partitioned between water (150 mL) and ethyl acetate (EtOAc, 250 mL). The organic phase was washed successively with: water (100 mL), a saturated solution of sodium carbonate (100 mL×2) and brine (100 mL×2), then dried over sodium sulfate, and concentrated under reduced pressure to afford a sticky oil. The sticky oil was triturated with MeOH (250 mL) and the precipitates were collected to give the intermediate 4 (6 g, 11.1 mmol, 83%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ ppm 4.52-4.46 (1H, m), 4.33 (1H, d, J=10.8 Hz), 4.06 (1H, d, J=11.2 Hz), 3.21-3.16 (1H, m), 2.86 (1H, dd, J=12.8, 3.2 Hz), 2.42-2.36 (1H, m), 2.05 (3H, s), 2.00 (3H, s), 1.94-0.84 (40H, m).

LC/MS: m/z calculated 540.4. found 563.3 (M+Na)+.

Step D: Intermediate 5

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(Hydroxymethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

A mixture of the intermediate 4 (7 g, 12.94 mmol) and potassium hydroxide (KOH, 0.872 g, 15.5 mmol) in EtOH (200 mL) and toluene (200 mL) was stirred vigorously at room temperature for 1 h. The reaction mixture was neutralized with aqueous HCl (1N) to pH 7 and evaporated to dryness. The obtained residue was taken up in water and a small amount of acetone. The precipitates were collected and then washed with water and dried in vacuo to obtain the intermediate 5 (6.0 g, 93%) as a white solid. LC/MS: m/z calculated 498.4. found 499.3 (M+1)+.

Step E: Intermediate 6

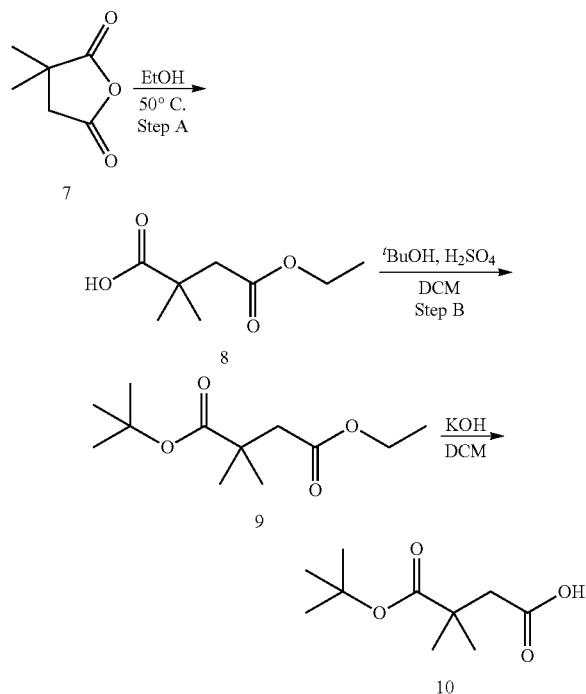
(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-Formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of the intermediate 5 (5.1 g, 10.23 mmol) in DCM (300 mL) at room temperature were added pyridinium chlorochromate (PCC, 6.61 g, 30.7 mmol), and silica gel (6.6 g). The reaction mixture was stirred at room temperature for 1 h. After the reaction was quenched with water, the organic phase was washed with saturated sodium bicarbonate solu-

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tion (100 mL), dried over sodium sulfate, and evaporated under reduced pressure to provide a crude product, which was purified by column chromatography on silica gel (EtOAc: PE=1:10 to 1:5) to provide the intermediate 6 (4.2 g, 83%) as a white solid. LC/MS: m/z calculated 496.4. found 497.2 (M+1)+.

Synthesis of the oxo-butanoate intermediate 10 was accomplished according to the following procedures.



Step A: Intermediate 8

4-Ethoxy-2,2-dimethyl-4-oxobutanoic acid

A solution of 3,3-dimethyl-dihydrofuran-2,5-dione 7 (25 g, 195 mmol) in anhydrous EtOH (150 mL) was stirred at 50° C. overnight. After cooling down to room temperature, the solvent was removed under reduced pressure with a rotary evaporator and the residue was triturated with hexane at -50° C. to afford the intermediate 8 (25 g, 133 mmol, 67.9%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ ppm 4.13-4.18 (2H, q, J=7.2 Hz), 2.62 (2H, s), 1.28 (6H, s), 1.32-1.25 (3H, t, J=7.6 Hz). LC/MS: m/z calculated 174.1. found 173.1 (M-1)-.

Step B: Intermediate 9

1-Tert-butyl 4-ethyl 2,2-dimethylsuccinate

To a mixture of the intermediate 8 (20 g, 109 mmol), magnesium sulfate (52.5 g, 436 mmol), and tert-butanol (60 mL) in DCM (480 mL) was added to sulfuric acid (8.72 mL, 164 mmol). After stirring at room temperature overnight, the reaction mixture was poured into saturated sodium bicarbonate solution (300 mL) and water (300 mL). DCM was added to extract the desired product, and the organic phase was washed with brine, dried, and concentrated to afford the intermediate 9 (19 g, 83 mmol, 80%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 4.02-4.08 (2H, q, J=7.2 Hz), 2.46

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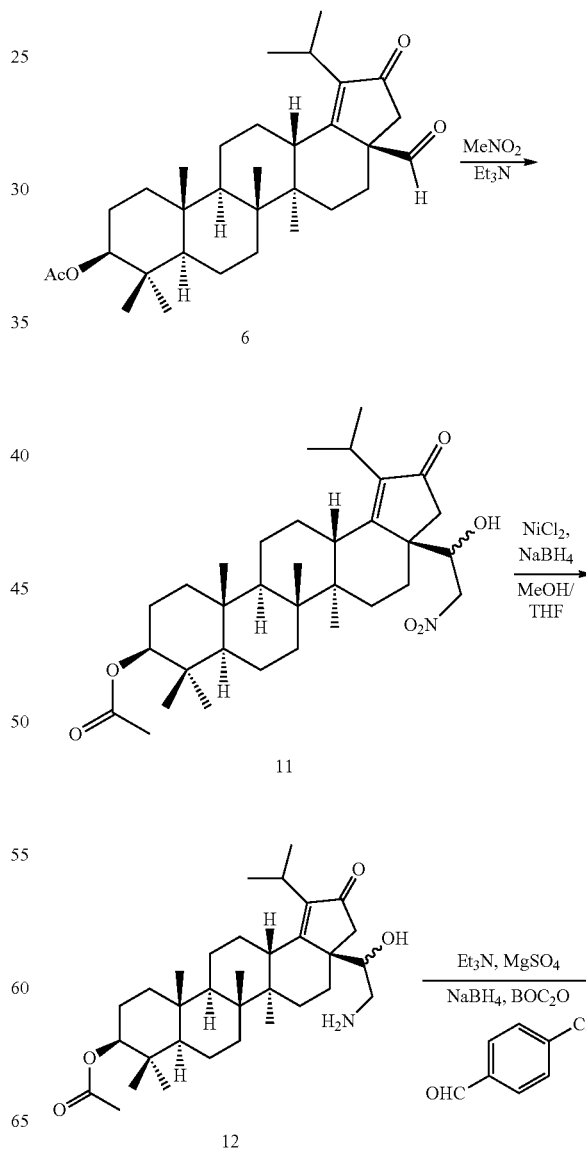
(2H, s), 1.07 (9H, s), 1.14-1.20 (9H, m). LC/MS: m/z calculated 230.2. found 253.1 (M+Na)+.

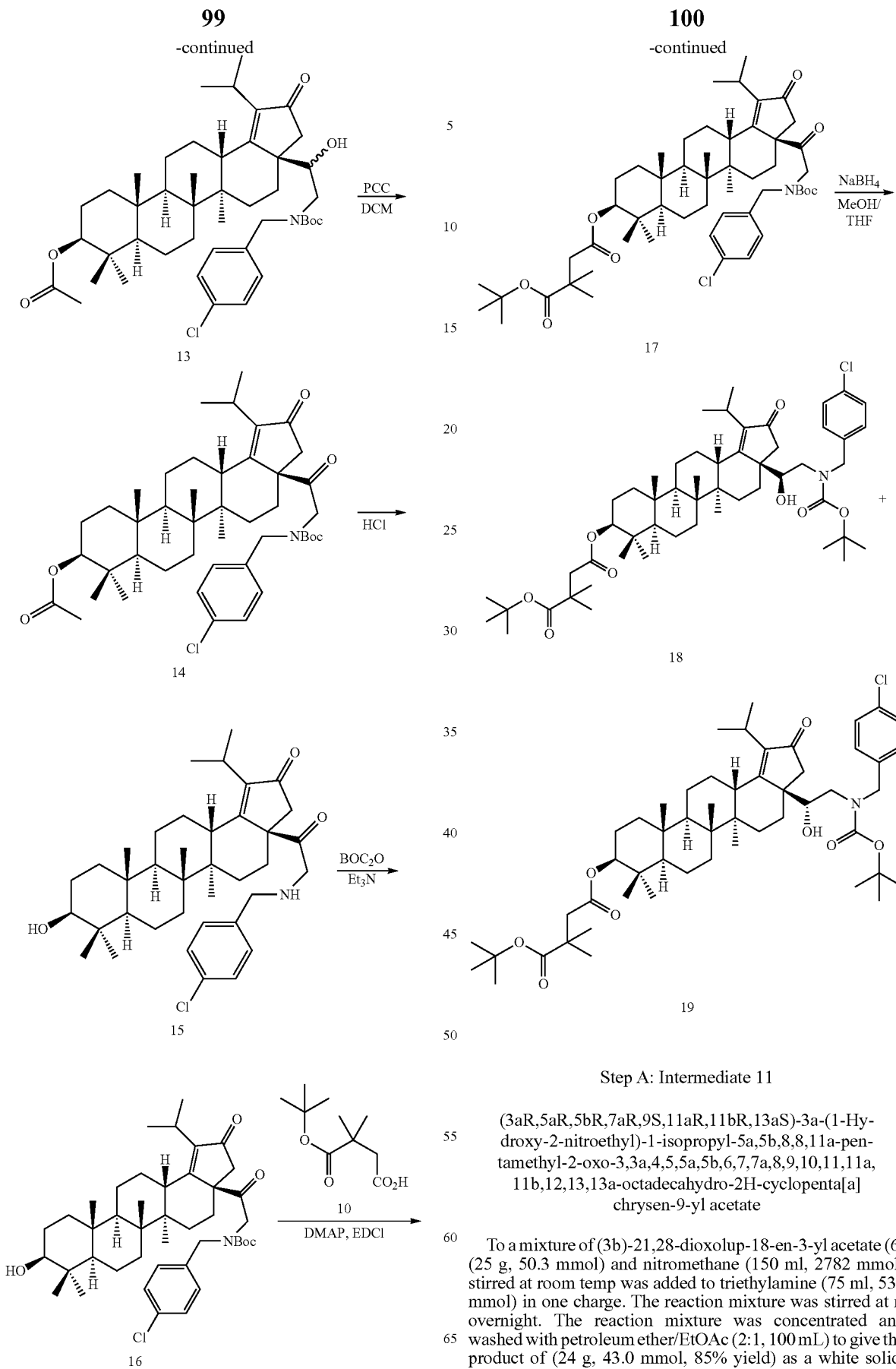
Step C: Intermediate 10

4-(Tert-butoxy)-3,3-dimethyl-4-oxobutanoic acid

To a solution of the intermediate 9 (10 g, 41.3 mmol) in EtOH (200 mL) was added to potassium hydroxide (12.86 g, 206 mmol) in water (100 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h. The pH of the reaction mixture was adjusted to 3-4 by 1N HCl. The resulting solution was extracted with ether (300 mL), and the ether phase was dried and concentrated to afford a crude product, which was re-crystallized from hexane at -10° C. to afford the intermediate 10 (4 g, 19.78 mmol, 47.9%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ ppm 2.58 (2H, s), 1.43 (9H, s), 1.25 (6H, s). LC/MS: m/z calculated 202.1. found 201.1 (M-1)-.

Synthesis of diastereomeric intermediates 18 and 19.





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Step B: Intermediate 12

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-Amino-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of 11 (15.0 g, 26.9 mmol) in methanol (300 mL) was added $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (9.59 g, 40.3 mmol) at -5°C . and was slowly added sodium borohydride (10.17 g, 269 mmol) at -5 to 10°C . (internal temp). The reaction mixture was stirred at -5°C . (bath temp) for 30 min. The mixture was then quenched with saturated NH_4Cl (200 mL), diluted with EtOAc (1500 mL), then stirred at rt overnight. And the organic layer was washed with saturated NH_4Cl (50 mL), water (800 mL), brine (800 mL) and was dried over MgSO_4 , filtered and concentrated to afford a solid, which was washed with petroleum ether to give the 12 (14 g, 24.40 mmol, 91% yield) as a white solid. LC/MS: m/z calculated 527.4. found 528.3 ($\text{M}+1$)⁺.

Step C: Intermediate 13

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((Tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of 12 (8 g, 14.58 mmol), triethylamine (0.813 ml, 5.83 mmol) and MgSO_4 (2.63 g, 21.87 mmol) in methanol (225 mL) stirred at rt was added 4-chlorobenzaldehyde (2.056 ml, 17.50 mmol). The reaction mixture was stirred at rt for 2 h, then cooled to -5°C . and NaBH_4 was added in small portions during 10 min and stirred for 30 min. Following this, Boc_2O (4.06 ml, 17.50 mmol) was added. The reaction was warmed to rt. and stirred for 1 h. The reaction mixture was poured into ice water (300 mL) and the solids were collected and dried to give 13 (7 g, 8.56 mmol, 58.7% yield) as a white foam. LC/MS: m/z calculated 751.5. found 774.3 ($\text{M}+\text{Na}$)⁺.

Step D: Intermediate 14

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((Tert-butoxycarbonyl)(4-chlorobenzyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a mixture of 13 (25 g, 29.9 mmol) in dichloromethane (200 mL), was added PCC (50 g, 232 mmol) and silica gel 50 g. This mixture was stirred at rt overnight. The solids were removed by filtration to obtain black solution, which was concentrated and purified by silica gel column chromatography eluting with hex/EtOAc (10:1) to afford the 14 (20 g, 23.99 mmol, 80% yield) as a white solid.

LC/MS: m/z calculated 749.4. found 772.2 ($\text{M}+\text{Na}$)⁺.

Step E: Intermediate 15

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-Chlorobenzyl)amino)acetyl)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-2-one

To a solution of 14 in 1,4-dioxane (200 mL) and methanol (200 mL) stirred at rt was added con HCl (100 mL) in one charge. The reaction mixture was stirred overnight at 45°C . The reaction mixture was concentrated and washed with acetone to give 15 (12.5 g, 17.45 mmol, 87% yield) as a white foam. LC/MS: m/z calculated 607.38. found 608.0 ($\text{M}+1$)⁺.

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Step F: Intermediate 16

Tert-butyl 4-chlorobenzyl(2-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-oxoethyl)carbamate

To a solution of 15 (6 g, 9.86 mmol) and Et_3N (5.50 mL, 39.5 mmol) in dichloromethane (30 mL) stirred at rt was added Boc_2O (2.290 mL, 9.86 mmol) in one charge. The reaction mixture was stirred at rt for 2 h. From TLC, the reaction was finished. The solvent was removed in vacuo. The crude product 16 (6 g, 8.47 mmol, 86% yield) was used without further purification.

Step G: Intermediate 17

4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((Tert-butoxycarbonyl)(4-chlorobenzyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate

To a solution of 10 (5.14 g, 25.4 mmol), DMAP (5.17 g, 42.3 mmol) and 16 (6 g, 8.47 mmol) in dichloromethane (50 mL) stirred at rt was added EDC (8.12 g, 42.3 mmol). The reaction mixture was stirred at rt until starting material disappeared as monitored by TLC. After the reaction was finished, the mixture was diluted with CH_2Cl_2 , and washed with aq NH_4Cl . The organic layer was dried with Na_2SO_4 and the solvent was removed in vacuo. The material was purified by silica gel chromatography (hex:EtOAc, 12:1 to 5:1) to give 17 (5.4 g, 6.05 mmol, 71.4% yield) as a light white solid. The proton NMR consists of a mixture of rotomers. ^1H NMR (400 MHz, CHLOROFORM-d) δ 7.34-7.24 (m, 2H), 7.23-7.08 (m, 2H), 4.63-4.29 (m, 3H), 4.11-3.39 (m, 2H), 3.28-3.06 (m, 1H), 2.69-0.69 (m, 68H).

Step H: Intermediates 18 and 19

4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((Tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate (18) & 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate (19)

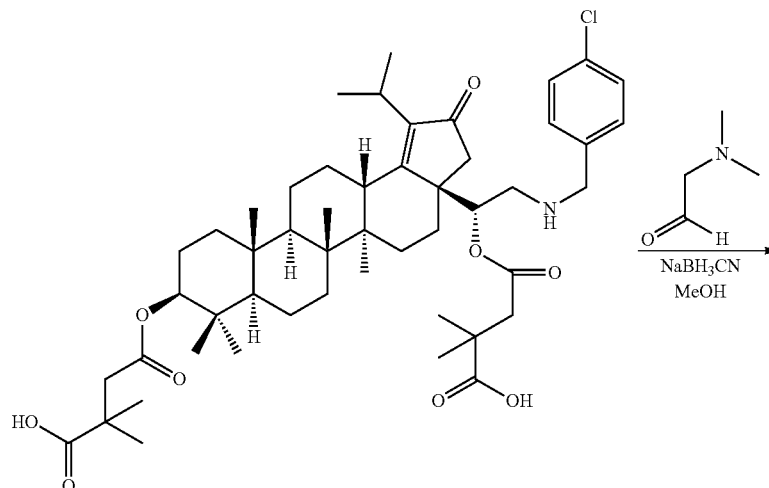
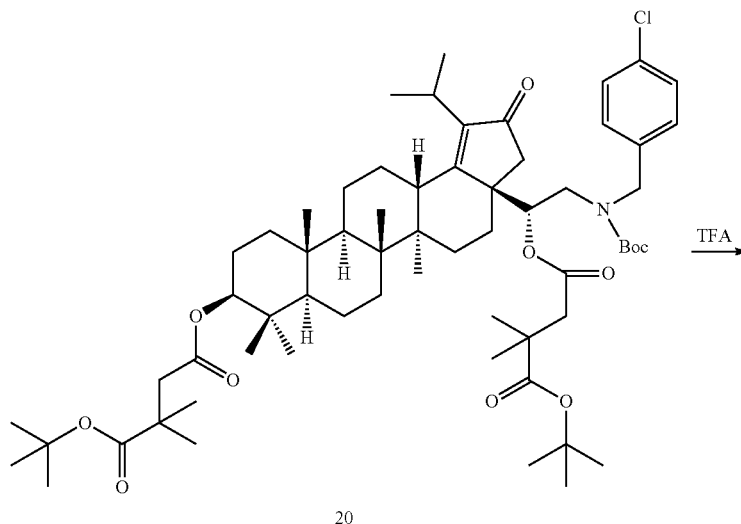
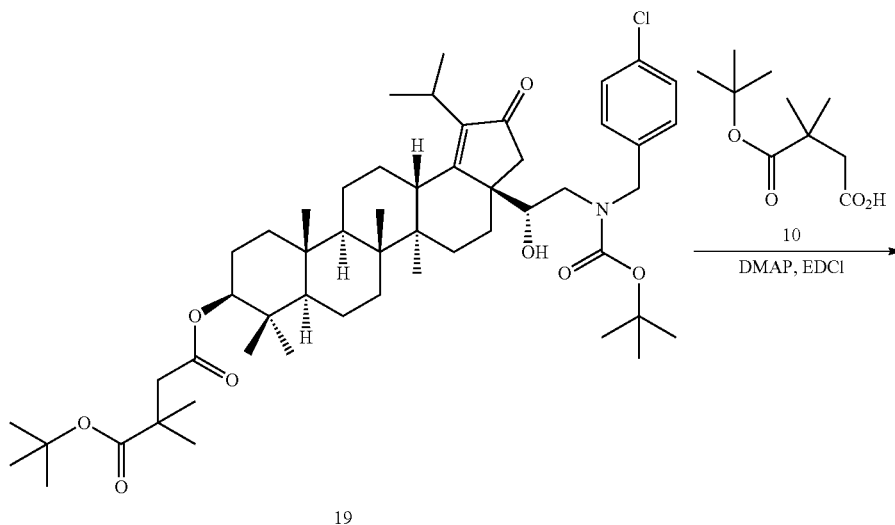
To a solution of 17 (1.5 g, 1.680 mmol) in methanol (10 mL) and THF (10.00 mL) stirred at 0°C . was added NaBH_4 (0.127 g, 3.36 mmol). The reaction mixture was stirred at 0°C . until starting material disappeared (about 2 hours) as monitored by TLC. Upon completion the mixture was diluted with water, extracted with EtOAc and the organic layer was dried with Na_2SO_4 . The residue was purified by silica gel chromatography (hex:EtOAc, 7:1 to 5:1) to give the diastereomer with the S configuration 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate (18) (700 mg, 0.782 mmol, 46.6% yield) and the diastereomer with the R configuration 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate (19) (500 mg, 0.559 mmol, 33.3% yield)

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both as a light white solids. For 18 ^1H NMR (400 MHz, CHLOROFORM- d) δ 7.40-7.24 (m, 2H), 7.18 (d, $J=8.3$ Hz, 2H), 4.87-4.57 (m, 1H), 4.51 (dd, $J=5.3, 11.0$ Hz, 1H), 4.42-4.13 (m, 2H), 3.43-3.05 (m, 3H), 2.97-2.78 (m, 1H), 2.62-2.47 (m, 2H), 2.47-2.29 (m, 1H), 2.01-0.70 (m, 64H);

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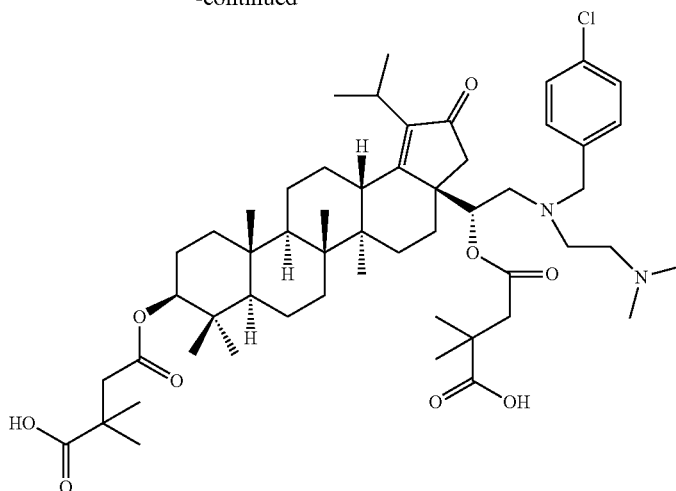
LC/MS: m/z calculated 893.6. found 916.5 ($\text{M}+\text{Na}$) $^+$. For 19 ^1H NMR (400 MHz, CHLOROFORM- d) δ 7.36-7.23 (m, 2H), 7.12 (d, $J=8.3$ Hz, 2H), 4.56-4.14 (m, 4H), 3.45-3.18 (m, 1H), 3.15-2.97 (m, 1H), 2.76-0.71 (m, 69H); LC/MS: m/z calculated 893.6. found 916.7 ($\text{M}+\text{Na}$) $^+$.



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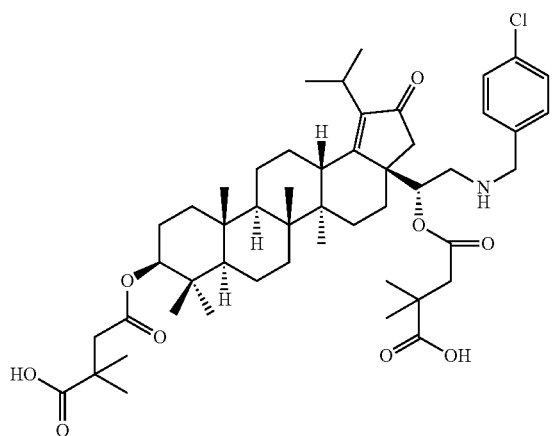
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Example 1
Compound 21

4-((R)-1-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-((3-Carboxy-3-methylbutanoyl)oxy)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-((4-chlorobenzyl)amino)ethoxy)-2,2-dimethyl-4-oxobutanoic acid



Step A: Intermediate 20

4-((R)-1-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-((4-(tert-butoxy)-3,3-dimethyl-4-oxobutanoyl)oxy)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)ethyl)-1-tert-butyl 2,2-dimethylsuccinate

To a solution of 10 (543 mg, 2.68 mmol), DMAP (205 mg, 1.677 mmol) in dichloromethane (5 mL) stirred at rt was added EDC (514 mg, 2.68 mmol). The reaction mixture was stirred at rt for 1 h. Then 19 (300 mg, 0.335 mmol) was added to the reaction mixture. Upon completion, the mixture was washed with 2 M HCl, water and brine. The organic layer was dried over Na₂SO₄ and concentrated to give the crude product 20 (400 mg, 0.278 mmol, 83% yield) as an oil. This material was used in the next step without further purification.

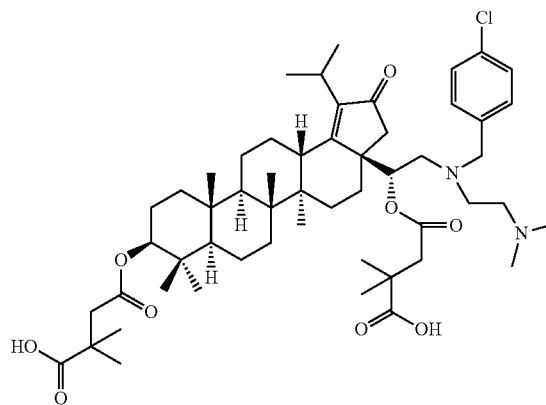
Step B: Compound 21

4-((R)-1-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-((3-Carboxy-3-methylbutanoyl)oxy)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-((4-chlorobenzyl)amino)ethoxy)-2,2-dimethyl-4-oxobutanoic acid

To a solution of 20 (400 mg, 0.371 mmol) in dichloromethane (5 mL) stirred at rt was added TFA (2 mL, 26.0 mmol). The reaction mixture was stirred at rt for 1 h. The mixture was evaporated to afford the TFA salt of intermediate 21 (350 mg, 0.343 mmol, 93% yield) as a light oil. ¹H NMR (400 MHz, CHLOROFORM-d) δ 7.33-7.12 (m, 4H), 5.76-5.60 (m, 1H), 4.48-4.32 (m, 1H), 4.26-3.98 (m, 2H), 3.18-2.89 (m, 2H), 2.89-2.68 (m, 2H), 2.69-0.60 (m, 58H); LC/MS: m/z calculated 865.5. found 866.3 (M+1)⁺.

Example 2
Compound 22

4-((R)-1-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-((3-Carboxy-3-methylbutanoyl)oxy)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethoxy)-2,2-dimethyl-4-oxobutanoic acid



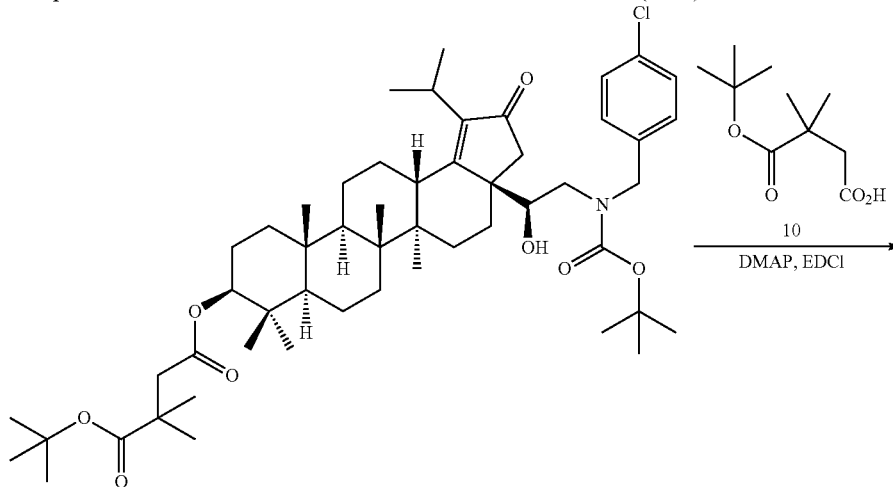
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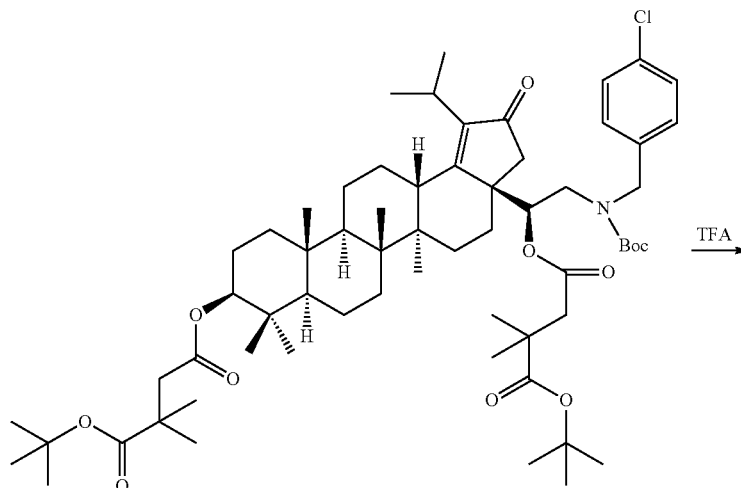
To a solution of 2-(dimethylamino)acetaldehyde, hydrochloride (441 mg, 3.57 mmol) in methanol (12 mL) was added 21, (as it's trifluoroacetic acid salt) (350 mg, 0.357 mmol). The mixture's pH was adjusted to 7-8 with Et₃N. The reaction mixture was stirred at rt for 2 h then NaBH₃CN (224 mg, 3.57 mmol) was added and mixture was stirred overnight. The reaction was filtered and evaporated to afford a crude

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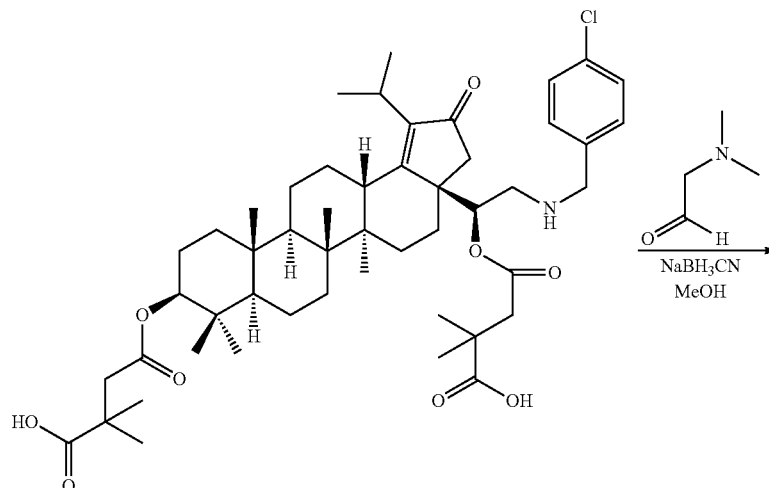
product. The residue was purified by preparative-HPLC to obtain compound 22 as a TFA salt (200 mg, 0.168 mmol, 47.2% yield) as a white solid. ¹H NMR (400 MHz, CHLOROFORM-d) δ 7.33 (d, J=8.3 Hz, 2H), 7.22 (d, J=8.3 Hz, 2H), 5.83-5.67 (m, 1H), 4.54-4.42 (m, 1H), 3.88-3.75 (m, 1H), 3.65-3.49 (m, 1H), 3.04-0.60 (m, 71H); LC/MS: m/z calculated 936.6, found 937.4 (M+1)⁺.



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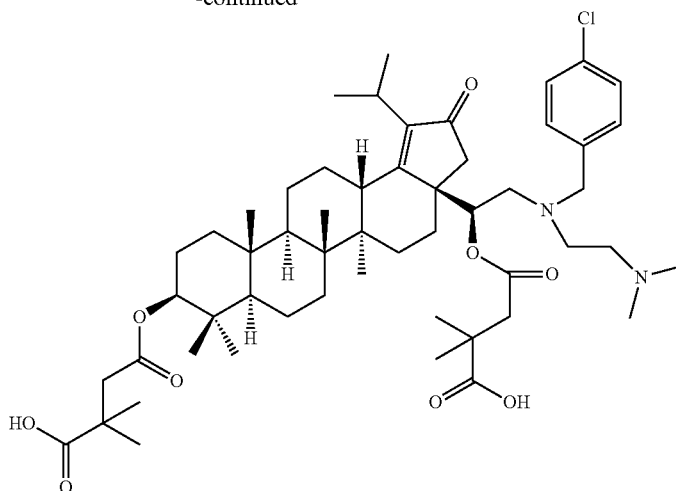


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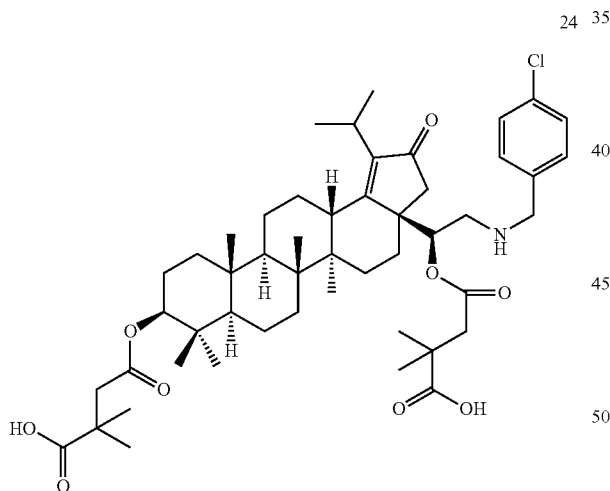


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Example 3

Compound 25

4-((S)-1-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-((3-Carboxy-3-methylbutanoyl)oxy)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethoxy)-2,2-dimethyl-4-oxobutanoic acid



Step A: Intermediate 23

4-((S)-1-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-((4-(Tert-butoxy)-3,3-dimethyl-4-oxobutanoyl)oxy)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)ethyl)-1-tert-butyl 2,2-dimethylsuccinate

To a solution of 10 (203 mg, 1.006 mmol), DMAP (123 mg, 1.006 mmol) in dichloromethane (10 ml) stirred at rt was added EDC (321 mg, 1.677 mmol). The reaction mixture was

stirred at rt for 1 h, then 18 (300 mg, 0.335 mmol) was added to the reaction. Upon completion, silica gel was added, the mixture was concentrated and purified by chromatography (petroleum ether:EtOAc 6:1 to 3:1) to give the 23 (344 mg, 0.319 mmol, 95% yield) as a light white solid.

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Step B: Compound 24

4-((S)-1-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-((4-(Tert-butoxy)-3,3-dimethyl-4-oxobutanoyl)oxy)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)ethyl)-1-tert-butyl 2,2-dimethylsuccinate

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To a solution of 23 (115 mg, 0.107 mmol) in DCM (5 mL) was added TFA (2.5 mL, 0.107 mmol). The reaction mixture was stirred at rt for 2 h and evaporated in vacuo to afford crude product. This material was then washed with satd. sodium bicarbonate solution, water and brine. The organics were filtered and concentrated to give the 24 (89 mg, 0.023 mmol, 21.17% yield) as a white solid. ¹H NMR (400 MHz, CHLOROFORM-d) δ 7.40 (s, 4H), 5.97-5.65 (m, 1H), 4.93-3.75 (m, 3H), 3.59-3.27 (m, 1H), 3.27-2.92 (m, 3H), 2.83-2.11 (m, 5H), 1.98-0.59 (m, 52H) LC/MS: m/z calculated 865.5. found 866.4 (M+1)⁺.

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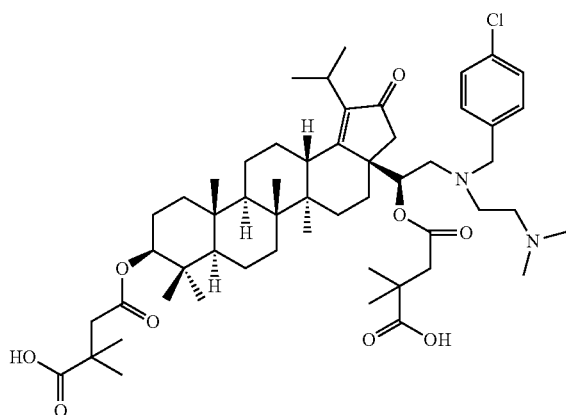
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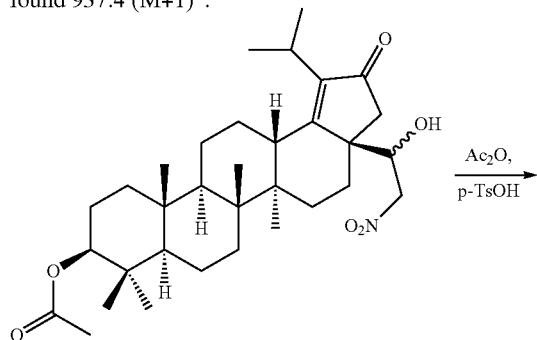
Example 4

Compound 25

4-((S)-1-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-((3-Carboxy-3-methylbutanoyl)oxy)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethoxy)-2,2-dimethyl-4-oxobutanoic acid



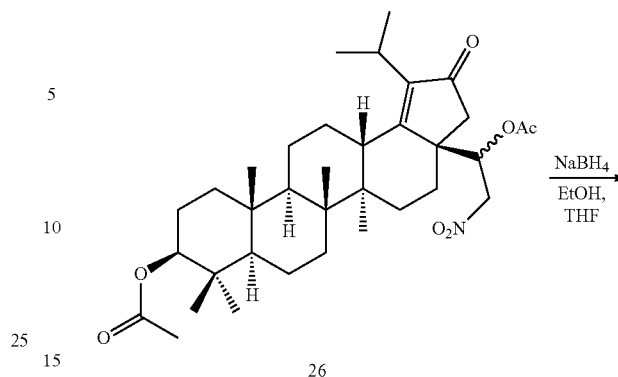
To a solution of 2-(dimethylamino)acetaldehyde (325 mg, 2.63 mmol) in methanol (5 ml) and DCE (50 ml) was added 24 (228 mg, 0.263 mmol) and triethylamine (0.110 ml, 0.789 mmol). The reaction mixture was stirred at rt for 3 h. The reaction was cooled to 0° C., and sodium cyanoborohydride (24.80 mg, 0.395 mmol) was added and resultant mixture was stirred overnight. The reaction was filtered and the filter cake was washed with DCM. The filtrate was concentrated under reduced pressure and the residue was purified by preparative-HPLC to give the title compound 25 as a TFA salt (76 mg, 0.065 mmol, 24.78% yield) as a white solid. ¹H NMR (400 MHz, CHLOROFORM-d) δ 7.38-7.30 (m, 2H), 7.30-7.19 (m, 2H), 5.82-5.69 (m, 1H), 4.53-4.44 (m, 1H), 4.05-3.89 (m, 1H), 3.70-3.54 (m, 1H), 3.41-2.51 (m, 15H), 2.45-2.12 (m, 2H), 1.97-0.65 (m, 54H); LC/MS: m/z calculated 936.6, found 937.4 (M+1)⁺.



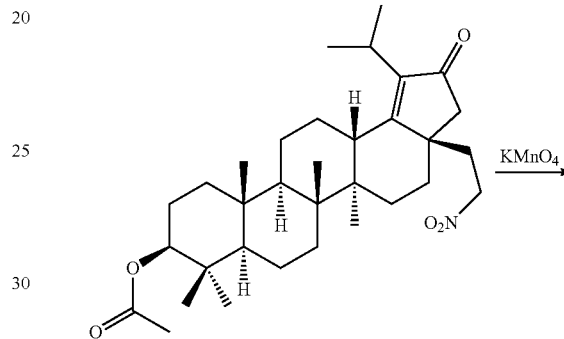
11

112

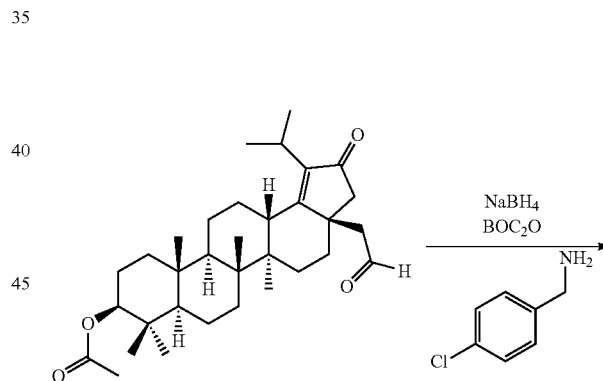
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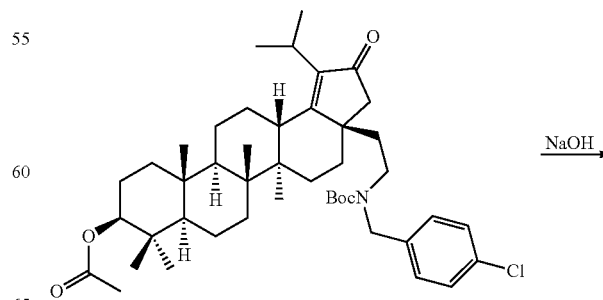
26



27



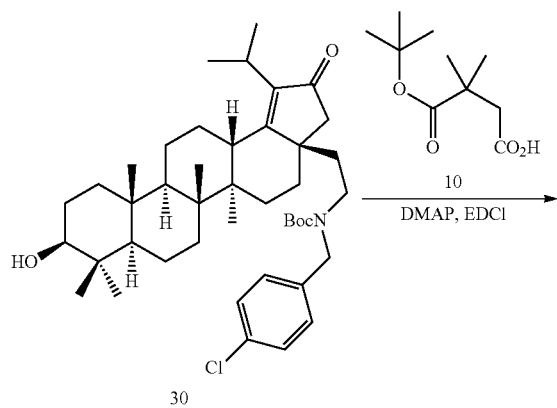
28



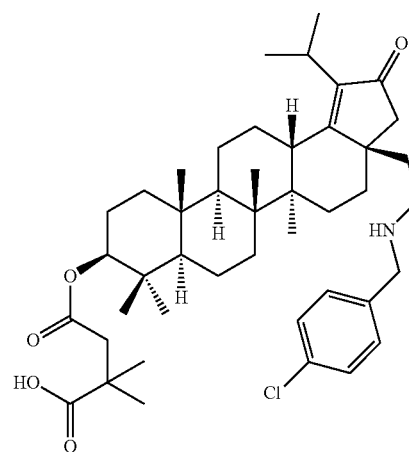
29

113

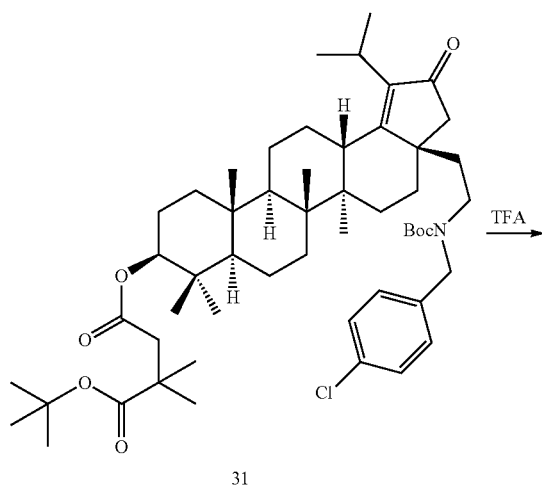
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**114**

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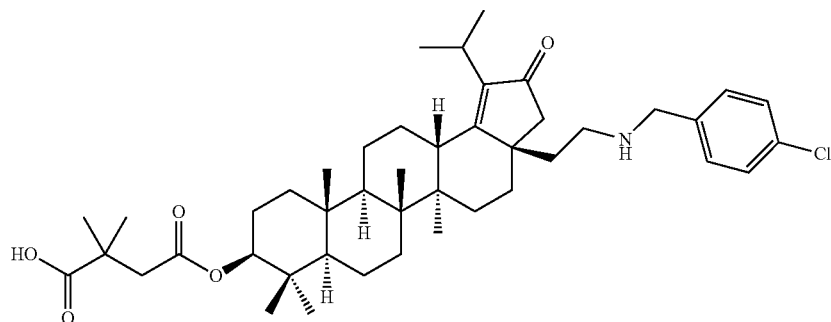
32



Example 5

Compound 32

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((4-Chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,
8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid



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Step A: Intermediate 26

1-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-Acetoxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-nitroethyl acetate

To a solution of 11 (20 g, 35.9 mmol) in acetic anhydride (100 mL, 1065 mmol) was added 4-methylbenzenesulfonic acid (1.852 g, 10.76 mmol). The reaction mixture was stirred at rt overnight. EtOAc (50 mL) and NaHCO₃ aq. (100 mL) were added. The organic layer was separated, washed with water, brine, and dried (Na₂SO₄). Removal of the solvent resulted in the crude product which was used directly in the next step. LC/MS: m/z calculated 599.4. found 600.3 (M+1)⁺.

Step B: Intermediate 27

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-Isopropyl-5a,5b,8,8,11a-pentamethyl-3a-(2-nitroethyl)-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of 26 (21 g, 35.0 mmol) in THF (30 mL) and EtOH (80 mL) in an ice bath was added NaBH₄ (5.30 g, 140 mmol). The mixture was then kept at rt for about 1 h, diluted with ethyl acetate (200 mL) and extracted with aqueous 10% citric acid solution (150 mL), saturated aqueous NaHCO₃ (150 mL), and brine (150 mL). The organic layer was dried (Na₂SO₄) and evaporated to give the crude product 27 (19 g, 27.2 mmol, 78% yield). This was used directly for the next step.

LC/MS: m/z calculated 541.4. found 542.3 (M+1)⁺.

Step C: Intermediate 28

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-Isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-oxoethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a stirred solution of 27 (10 g, 18.46 mmol) in acetone (90.00 mL) and methanol (90 mL) at -5° C. was added dropwise a solution of KOH (1.036 g, 18.46 mmol) in 5 mL water, then followed by KMnO₄ (1.896 g, 12.00 mmol) and MgSO₄ (1.666 g, 13.84 mmol) in 90 mL of water. The temperature was held below 0° C. for 1 h and for another 1 h at room temperature. The reaction mixture was diluted with DCM (100 mL), then filtered on CELITE® and washed with DCM. The organic phase was concentrated, then extracted with DCM, to give the crude product 28 (5 g, 8.12 mmol, 44.0% yield) which was used directly for the next step without further purification. ¹H NMR (400 MHz, CHLOROFORM-d) 9.64 (s, 1H), 4.49 (dd, J=5.5, 11.0 Hz, 1H), 3.27-3.06 (m, 1H), 2.87-2.76 (m, 1H), 2.76-2.64 (m, 1H), 2.64-2.54 (m, 1H), 2.45 (d, J=18.8 Hz, 1H), 2.20 (d, J=18.8 Hz, 1H), 2.05 (s, 3H), 1.99-0.67 (m, 39H); LC/MS: m/z calculated 510.4. found 533.3 (M+Na)⁺.

Step D: Intermediate 29

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((Tert-butoxycarbonyl)(4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of 28 (1.5 g, 2.94 mmol), TEA (0.164 mL, 1.175 mmol) and MgSO₄ (0.530 g, 4.41 mmol) in methanol

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(15 mL) stirred at rt was added 4-chlorobenzylamine (0.487 mL, 4.11 mmol). The reaction mixture was stirred at 20° C. for 2 h, then cooled to -5° C. and NaBH₄ (0.167 g, 4.41 mmol) was added in small portions during 10 min and stirred for 30 min. BOC₂O (0.750 mL, 3.23 mmol) was then added. The reaction was warmed to rt and stirred for 1 h. The reaction mixture was poured into ice water (300 mL) and solids were collected and dried to give 29 (1.8 g, 2.106 mmol, 72%) as a white foam. This material was used without further purification. LC/MS: m/z calculated 735.5. found 758.3 (M+Na)⁺.

Step E: Intermediate 30

Tert-butyl 4-chlorobenzyl(2-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)ethyl)carbamate

To a solution of 29 (1.6 g, 2.173 mmol) in methanol (6 mL) and THF (6 mL), and water (6 mL) was added NaOH (5.21 g, 130 mmol). The reaction mixture was stirred at rt for 1 h. Water and EtOAc were added upon completion and the layers separated. The organic layer was washed with water, brine, and dried (Na₂SO₄). Removal of the solvent gave 30 (1.4 g, 1.590 mmol, 73%) as a white solid.

LC/MS: m/z calculated 693.5. found 716.3 (M+Na)⁺.

Step F: Intermediate 31

4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((Tert-butoxycarbonyl)(4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate

To a solution of DMAP (0.862 g, 7.06 mmol), EDC (1.932 g, 10.08 mmol) and 4-tert-butoxy-3,3-dimethyl-4-oxobutanoic acid (10) (1.631 g, 8.06 mmol) in DCM (60 mL) stirred at 20° C. for 30 min was added 30 (1.4 g, 2.016 mmol). The reaction mixture was stirred at 20° C. for 1 h. The mixture was washed with saturated ammonium chloride, water, and saturated NaHCO₃, water, and lastly brine. The organic layer was dried over Na₂SO₄, filtered and concentrated to give the crude product, which was purified by silica gel column eluting with petrol ether/Ethyl acetate (4:1) to afford the product 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate (1.4 g, 0.986 mmol, 49%) as a yellow solid.

Step G: Compound 32

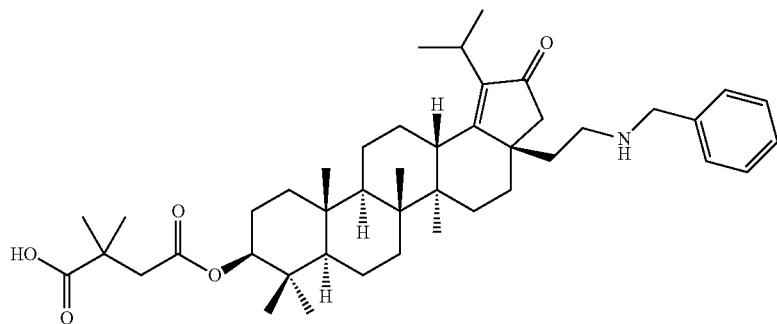
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-Chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

To a solution of 31 (1.4 g, 1.593 mmol) in DCM (6 mL) was added TFA (3 mL). The reaction mixture was stirred at 20° C. for 2 h and evaporated in vacuo to afford crude product which was purified by preparative-HPLC to give the title compound trifluoroacetic acid salt (1 g, 73%) as a white solid. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.57-7.42 (m, 4H), 4.51 (dd, J=5.1, 11.2 Hz, 1H), 4.29-4.15 (m, 2H), 3.30-3.18 (m, 1H), 2.98-2.69 (m, 3H), 2.62 (q, J=16.0 Hz, 2H), 2.29 (d, J=19.1 Hz, 1H), 2.17-0.79 (m, 48H); LC/MS: m/z calculated 721.5. found 722.3 (M+1)⁺.

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Example 6
Compound 33

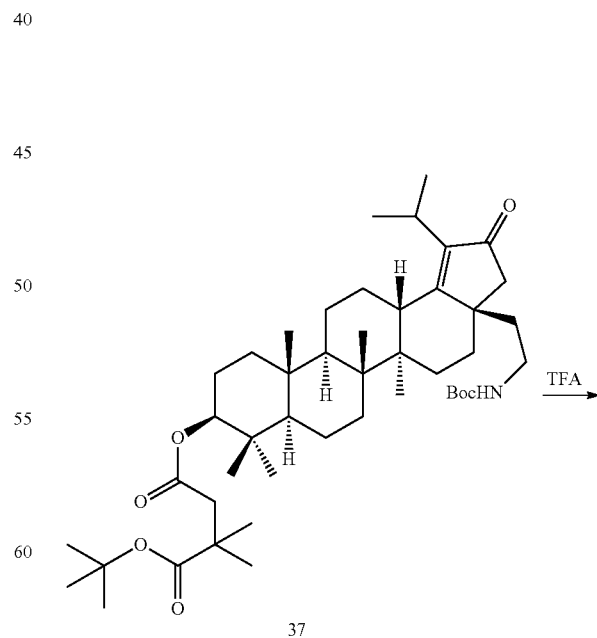
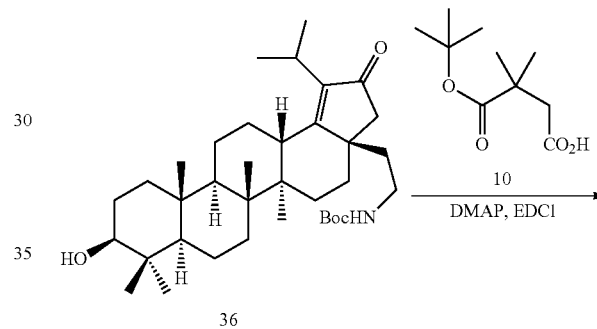
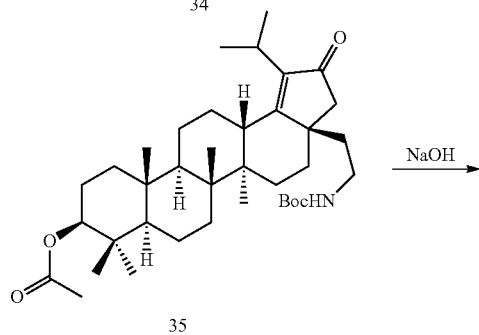
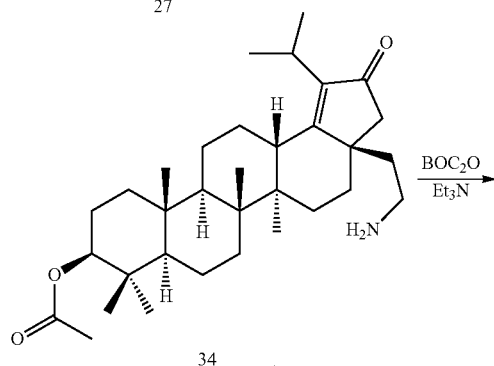
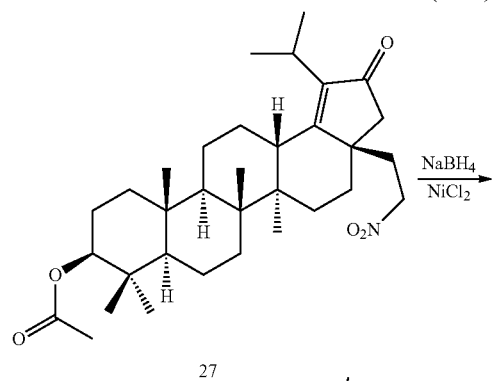
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-(Benzylamino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

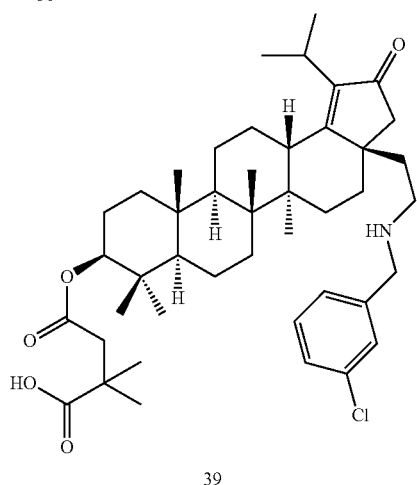
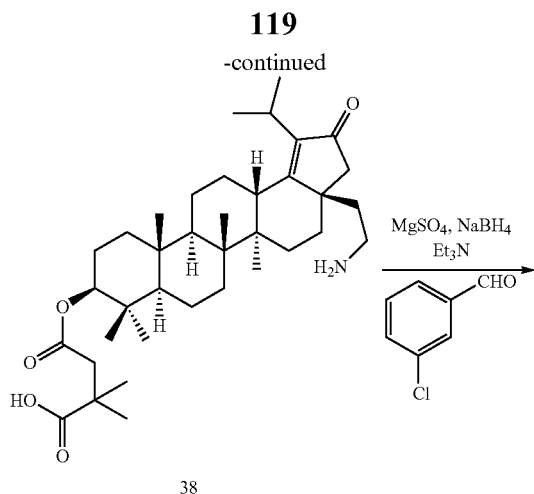


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The title compound was made in a similar manner to example 5 as a TFA salt. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.48 (s, 5H), 4.51 (dd, J=5.1, 11.2 Hz, 1H), 4.30-4.17 (m, 2H), 3.31-3.19 (m, 1H), 2.96-2.71 (m, 3H), 2.62 (q, J=15.9 Hz, 2H), 2.29 (d, J=18.8 Hz, 1H), 2.21-0.78 (m, 48H); LC/MS: m/z calculated 687.5. found 688.4 (M+1)⁺.

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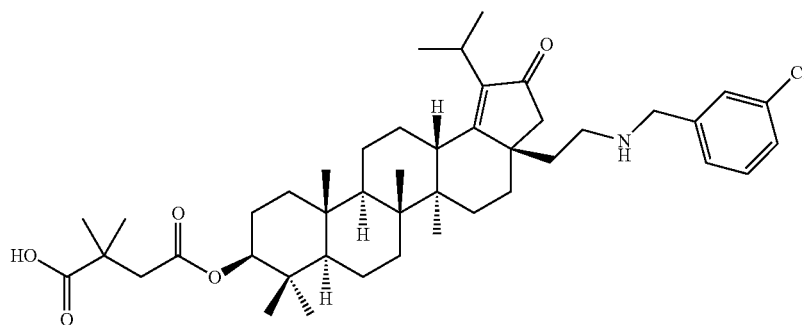




Example 7

Compound 39

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((3-Chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



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Step A: Compound 34

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-Aminoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3a-(2-nitroethyl)-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (27) (10 g, 18.46 mmol) and nickel(II) chloride (7.18 g, 55.4 mmol) in methanol (100 ml) was added sodium borohydride (6.98 g, 185 mmol) portionwise during 1 hour. The reaction mixture was stirred at 0° C. for 1 h. The mixture was diluted with EtOAc (250 mL). The organic phase was washed with sat. NH₄Cl (50 mL) until the organic layer change to colorless. The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated in vacuo to get the crude product (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-aminoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (34) (7 g, 12.63 mmol, 68.4% yield), which was used without further purification. ¹H NMR (400 MHz, CHLOROFORM-d) δ=9.15 (dd, J=4.9, 11.4 Hz, 1H), 8.12 (br. s., 2H), 7.97-7.81 (m, 1H), 7.63-7.49 (m, 1H), 7.26-7.15 (m, 1H), 7.15-7.04 (m, 1H), 6.98 (d, J=18.6 Hz, 1H), 6.81-5.38 (m, 47H); LC/MS: m/z calculated 511.4, found 512.3 (M+1)⁺.

Step B: Compound 35

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((Tert-butoxycarbonyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-aminoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (34) (5.3 g, 10.36 mmol), TEA (2.165 mL, 15.53 mmol) and TEA (2.165 mL, 15.53 mmol) in dichloromethane (DCM) (100 mL) stirred at room temp was added BOC₂O (2.404 mL, 10.36 mmol). The reaction mixture was stirred at 20° C. for 2 h. The reaction mixture was poured into ice water (300 ml) and the solids were collected and dried to give (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (35)

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(5.8 g, 8.34 mmol, 81% yield) as a white foam. This was used crude in next reaction without further purification. ¹H NMR (400 MHz, CHLOROFORM-d) δ =4.58-4.37 (m, 2H), 3.26-2.96 (m, 4H), 2.93-2.72 (m, 2H), 2.28 (d, J=18.8 Hz, 1H), 2.11-0.71 (m, 53H); LC/MS: m/z calculated 611.5. found 634.3 (M+Na)⁺.

Step C: Compound 36

Tert-butyl (2-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)ethyl)carbamate

A solution of (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (35) (5.8 g, 9.48 mmol), NaOH (11.37 g, 284 mmol) in methanol (4 mL), THF (6 mL), and Water (2 mL) was stirred at room temperature for 1 h. EtOAc was added and the reaction mixture was washed with water. The organic layer was separated, washed with water and brine, and dried (Na₂SO₄). Removal of the solvent provide tert-butyl (2-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)ethyl)carbamate (36) (5.4 g, 7.87 mmol, 83% yield) as a white solid. ¹H NMR (400 MHz, CHLOROFORM-d) δ =4.53-4.36 (m, 1H), 3.30-2.94 (m, 4H), 2.94-2.67 (m, 2H), 2.28 (d, J=18.8 Hz, 1H), 2.11-0.55 (m, 50H); LC/MS: m/z calculated 569.4. found 592.3 (M+Na)⁺.

Step D: Compound 37

4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate

A solution of 4-tert-butoxy-3,3-dimethyl-4-oxobutanoic acid (10) (4.79 g, 23.69 mmol), DMAP (3.47 g, 28.4 mmol) and tert-butyl (2-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)ethyl)carbamate (36) (5.4 g, 9.48 mmol) EDC (9.08 g, 47.4 mmol) in dichloromethane (DCM) (25 mL) was stirred at rt overnight. NH₄Cl was added and the mixture was extracted with DCM, and purified by chromatography with PE:EA (10:1) to give the 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate (37) (6.7 g, 8.75 mmol, 92% yield). ¹H NMR (400 MHz, CHLOROFORM-d) δ =4.62-4.39 (m, 2H), 3.24-3.10 (m, 1H), 3.10-2.93 (m, 1H), 2.93-2.68 (m, 2H), 2.62-2.49 (m, 1H), 2.28 (d, J=18.8 Hz, 1H), 2.11-0.69 (m, 66H); LC/MS: m/z calculated 753.6. found 776.5 (M+Na)⁺.

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Step E: Compound 38

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-Aminoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

To a solution of 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate (37) (6.7 g, 8.88 mmol) in DCM (20 mL) stirred at rt was added TFA (4 mL, 51.9 mmol). The reaction mixture was stirred at rt for 2 h. The reaction mixture was washed with sat. NaHCO₃. A solid was formed and collected by filtration to give 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-aminoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (38) (4 g, 6.55 mmol, 73.7% yield) as a white solid. ¹H NMR (400 MHz, DMSO-d₆) δ =4.44-4.28 (m, 1H), 3.20-3.05 (m, 1H), 2.87-2.75 (m, 1H), 2.46-2.16 (m, 6H), 1.97-0.66 (m, 47H);

LC/MS: m/z calculated 597.4. found 598.3 (M+1)⁺.

Step F: Compound 39

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((3-Chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

To a solution of 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-aminoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (38) (300 mg, 0.502 mmol), TEA (0.028 mL, 0.201 mmol) and MgSO₄ (91 mg, 0.753 mmol) in methanol (15 mL) stirred at room temp was added 3-chlorobenzaldehyde (85 mg, 0.602 mmol). The reaction mixture was stirred at 20° C. for 2 h. The reaction mixture was then cooled to 0° C. and NaBH₄ (1.541 g, 40.7 mmol) was added in portions within 30 min, after which the solution was allowed to stirred for 1 h. The mixture was purified by preparative-TLC eluting with DCM/MeOH (20:1) to give 39 (108 mg, 0.147 mmol, 29%). ¹H NMR (500 MHz, METHANOL-d₄) δ =7.41 (s, 1H), 7.38-7.24 (m, 3H), 4.48 (dd, J=5.7, 10.7 Hz, 1H), 3.89-3.67 (m, 2H), 3.26-3.11 (m, 1H), 2.84-2.73 (m, 1H), 2.66-2.47 (m, 2H), 2.46-2.34 (m, 1H), 2.34-2.21 (m, 2H), 2.08-0.77 (m, 48H).

123

Example 8

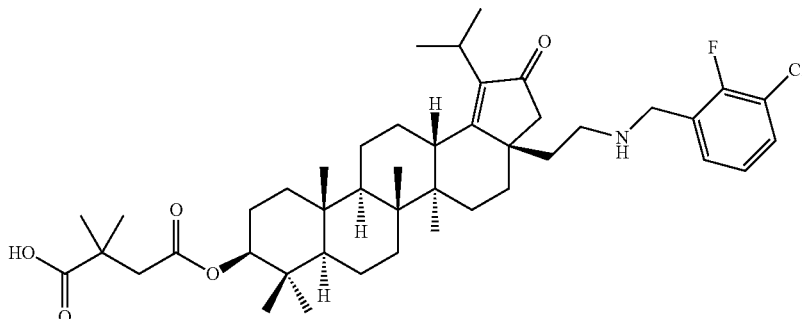
Compound 40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,113aS)-3a-(2-
((3-Chloro-2-fluorobenzyl)amino)ethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

124

40



The title compound was made in a similar manner to Example 7, but as a TFA salt. ¹H NMR (500 MHz, METHANOL-d₄) δ=7.46-7.38 (m, 1H), 7.35 (t, J=6.6 Hz, 1H), 7.17 (t, J=7.7 Hz, 1H), 4.48 (dd, J=5.5, 10.6 Hz, 1H), 3.97-3.72 (m, 2H), 3.27-3.12 (m, 1H), 2.85-2.73 (m, 1H), 2.67-2.45 (m, 2H), 2.44-2.16 (m, 3H), 2.09-0.73 (m, 48H).

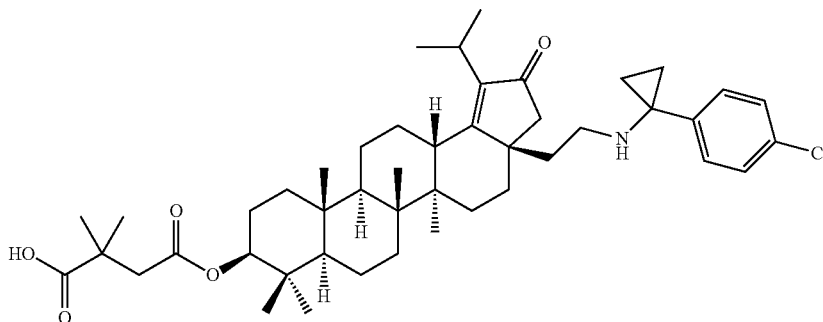
Example 9

Compound 41

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((1-(4-chlorophenyl)cyclopropyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

30 butoxy)-3,3-dimethyl-4-oxobutanoic acid (10) (0.988 g, 4.89 mmol), EDC (1.171 g, 6.11 mmol) and DMAP (0.522 g, 4.28 mmol) in DCM (12 mL) stirred at room temp was added tert-butyl (1-(4-chlorophenyl)cyclopropyl)(2-((3aR,5aR, 35 5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a, 5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10, 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a] chrysen-3a-yl)ethyl)carbamate (1.1 g, 1.221 mmol). The reaction mixture was stirred at rt for 2 h. Next, TFA (6 mL) 40 was added to the reaction mixture. Then, the reaction solution was stirred at rt for another 1.5 h, and the product was extracted with DCM (60 mL*3), and the combined organic phase was washed with brine (100 ml), dried over Na₂SO₄, concentrated and the residue was purified by recrystallization 45 from DCM and hexane (1:6) resulting in 800 mg of the TFA salt of 41 as white solid. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.64-7.44 (m, 4H), 4.50 (dd, J=5.1, 11.2 Hz, 1H),

41

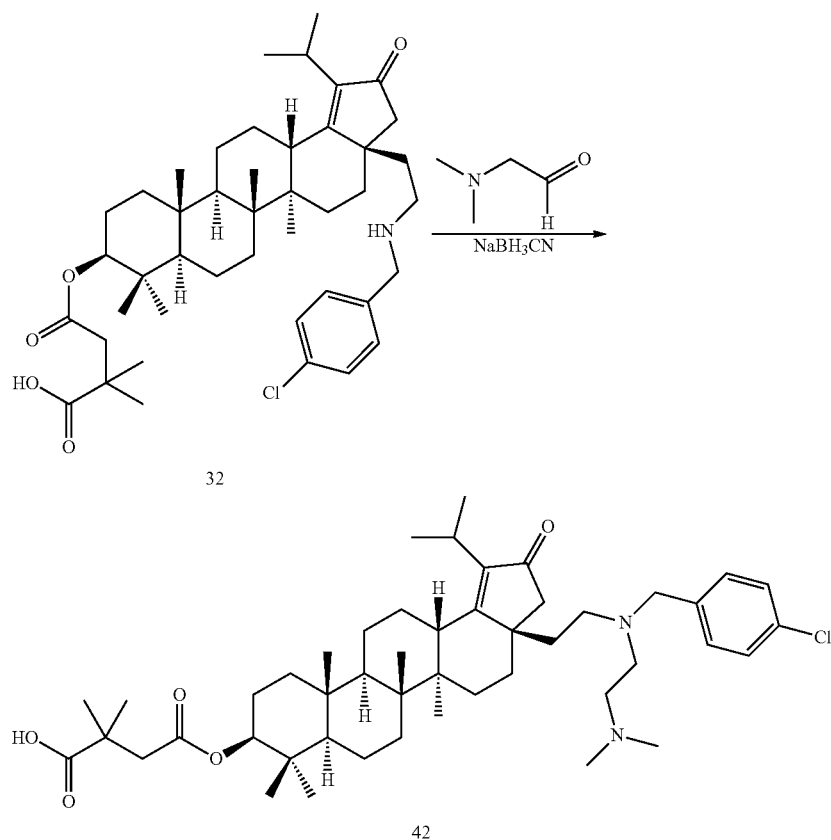


The title compound was made in a similar manner to Example 5, but as a TFA salt. The final step was performed according to the following procedure. To a solution of 4-(tert-

65 3.26-3.10 (m, 1H), 2.84-2.41 (m, 5H), 2.24-2.12 (m, 1H), 2.12-0.78 (m, 52H); LC/MS: m/z calculated 747.5. found 748.3 (M+1)⁺.

125

126

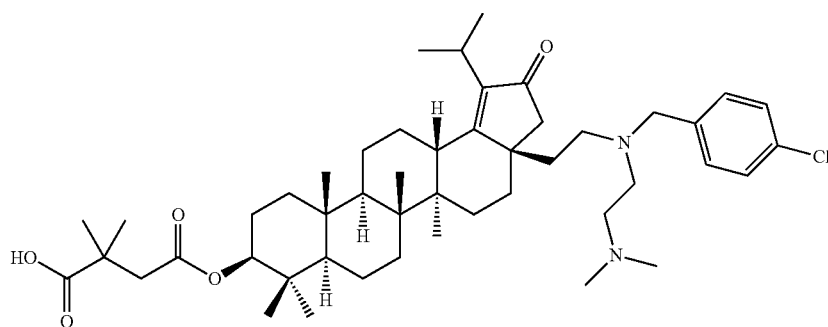


Example 10

Compound 42

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

35 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid, hydrochloride (32) (300 mg, 0.395 mmol). The reaction mixture was stirred at 40° C. for 2 h. The reaction was cooled to rt and sodium cyanoborohydride (24.84 mg, 0.395 mmol) was added and the resultant solution was stirred overnight. The reaction was diluted with ammonium chloride (40 ml), and extracted with DCM (60 ml×3). The combined organic layers were washed with brine (20 ml), dried over sodium sulfate, filtered and concentrated in vacuo. The residue was purified by preparative-HPLC to afford 42 as a trifluoroacetic acid salt (200 mg, 49% yield) as



To a solution of 2-(dimethylamino)acetaldehyde (244 mg, 1.977 mmol) in methanol (100 ml) was added 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-

a white solid. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.52-7.34 (m, 4H), 4.50 (dd, J=5.0, 11.0 Hz, 1H), 4.07-3.88 (m, 1H), 3.83-3.62 (m, 1H), 3.53-3.35 (m, 2H), 3.22-2.89 (m, 9H), 2.71-2.54 (m, 2H), 2.50-2.21 (m, 4H), 2.06-0.83 (m, 48H); LC/MS: m/z calculated 792.5. found 793.4 (M+1)⁺.

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Example 11

Compound 43

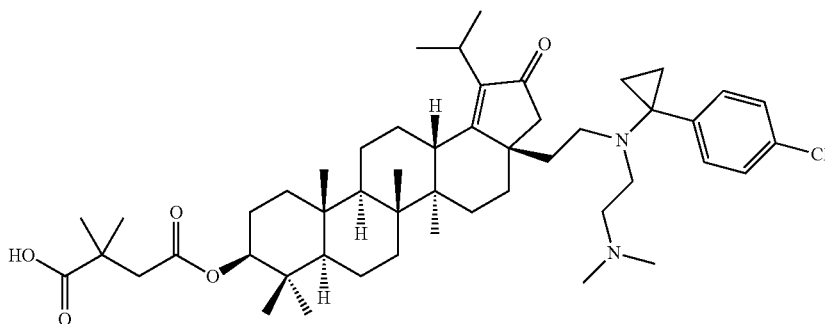
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((1-(4-Chlorophenyl)cyclopropyl) (2-(dimethyl-
 amino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid

5

10

128

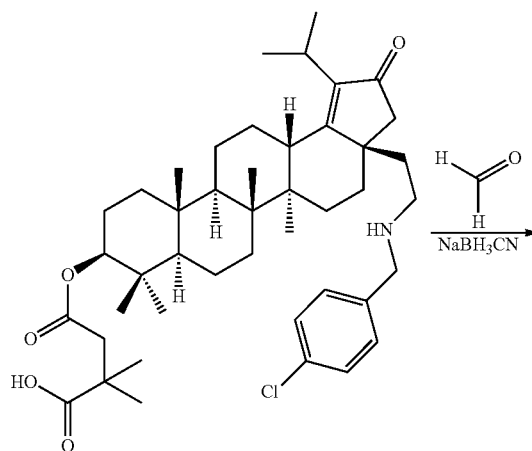
43



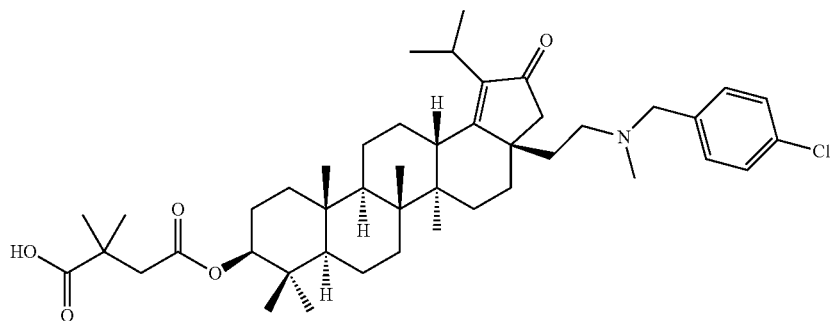
The title compound was made in a similar manner to
 Example 10, as a TFA salt. ¹H NMR (400 MHz, METHA-
 NOL-d₄) δ=7.35 (s, 4H), 4.51 (dd, J=5.1, 11.2 Hz, 1H), 3.31-

3.17 (m, 2H), 3.12-2.73 (m, 9H), 2.73-2.51 (m, 2H), 2.44-
 2.17 (m, 3H), 2.14-0.77 (m, 53H); LC/MS: m/z calculated
 818.4. found 819.4 (M+1)⁺.

30



32

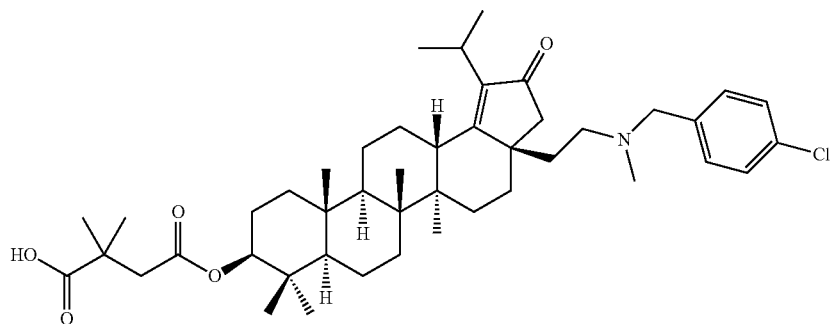


44

Compound 44

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((4-Chlorobenzyl)(methyl)amino)ethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

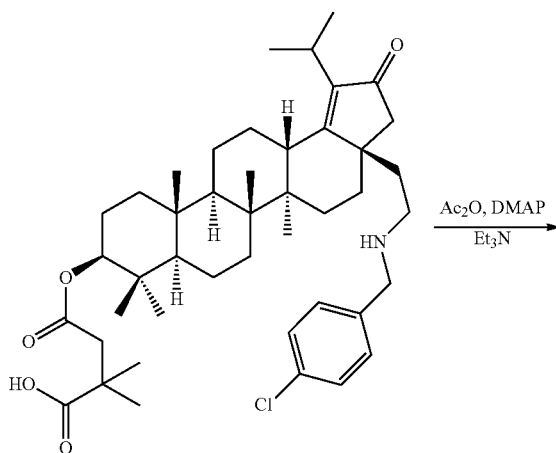


44

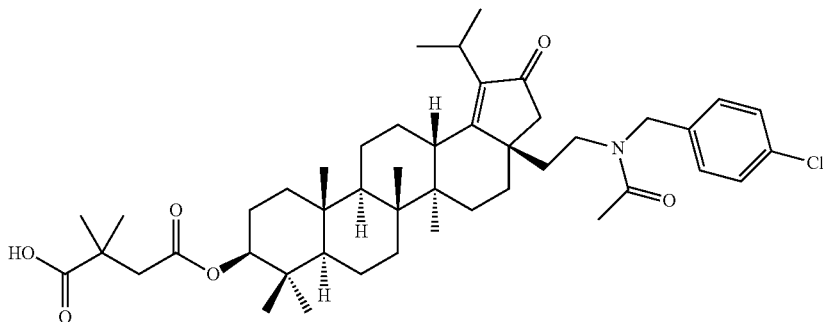
To a solution of 32 (150 mg, 0.208 mmol) in MeOH (6 mL) at rt was added formaldehyde (33.7 mg, 0.415 mmol). The reaction mixture was stirred at rt for 2 h. NaCNBH₄ (104 mg, 1.661 mmol) was added portionwise and the mixture stirred for overnight. The solvent was evaporated, and the mixture was purified by preparative HPLC to provide the TFA salt of

44 (60 mg, 34%). ¹H NMR (400 MHz, METHANOL-d₄) δ=7.60-7.44 (m, 4H), 4.56-4.37 (m, 2H), 4.36-4.24 (m, 1H), 3.28-3.14 (m, 1H), 2.89 (m, 5H), 2.73-2.50 (m, 2H), 2.28 (d, J=19.1 Hz, 1H), 2.20-0.83 (m, 49H); LC/MS: m/z calculated 735.5, found 736.3 (M+1)⁺.

30



32



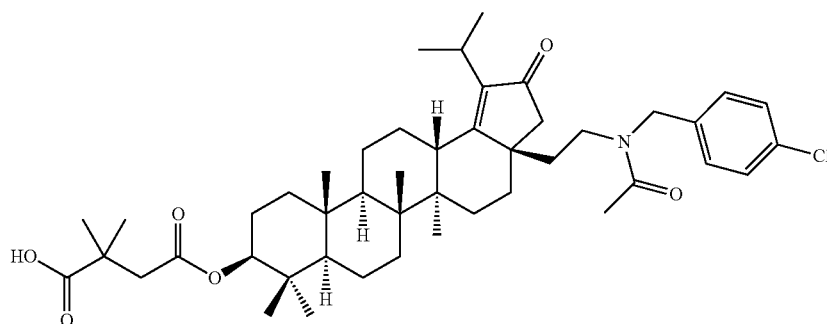
45

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Example 13

Compound 45

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(N-(4-Chlorobenzyl)acetamido)ethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid



45

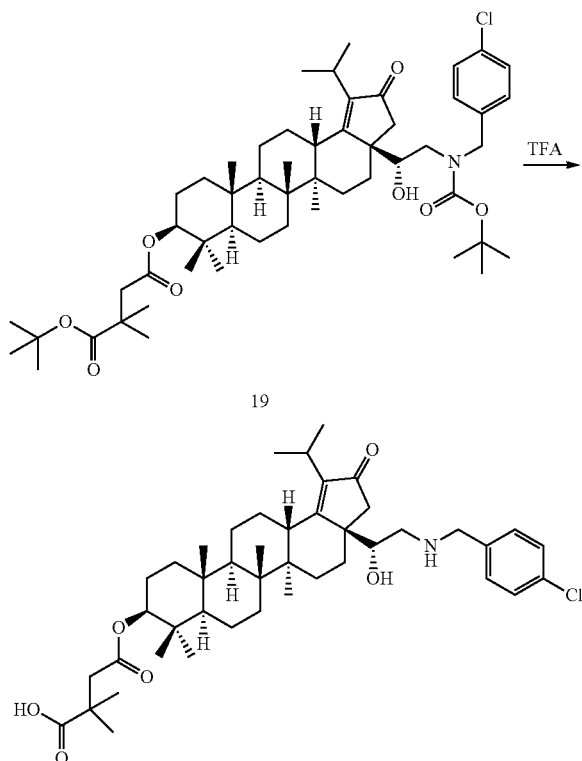
A mixture of 32 (150 mg, 0.208 mmol), TEA (210 mg, 2.076 mmol) and DMAP (5 mg, 0.042 mmol) in DCM (5 ml) was stirred for 3 hours. Next, the mixture was quenched with water (50 ml). The organics were then washed with water (2x50 ml), dried over Na₂SO₄, and evaporated in vacuo to afford crude product. This was then purified by preparative HPLC to give 45 (65 mg, 0.085 mmol, 41%) as a white solid. Mixture of rotomers. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.49-7.18 (m, 4H), 4.80-4.42 (m, 3H), 3.27-2.81 (m, 4H), 2.76-2.52 (m, 2H), 2.36-2.10 (m, 4H), 2.08-0.82 (m, 48H); LC/MS: m/z calculated 763.5, found 764.3 (M+1)⁺.

Example 14

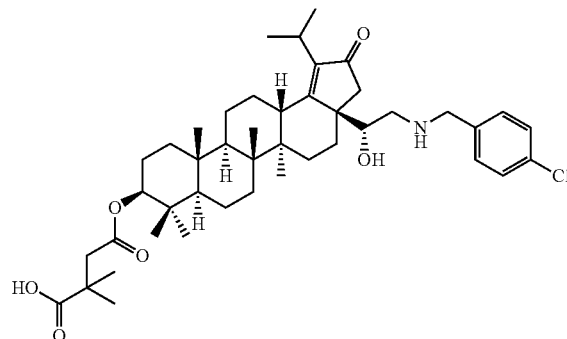
Compound 46

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-Chlorobenzyl)amino)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

46



46



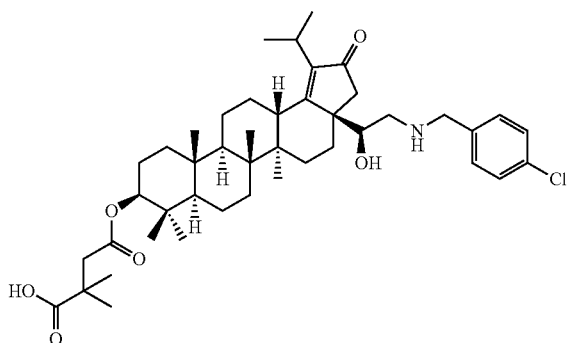
To a solution of 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate (19) (300 mg, 0.335 mmol) in DCM (30 mL) stirred at rt was added TFA (15 mL, 195 mmol). The reaction mixture was stirred at rt until LCMS and TLC indicated SM disappeared. The solvent was removed in vacuo and the residue was purified by preparative HPLC to give 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-Chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (46) (100 mg, 0.135 mmol, 40.4% yield) as a TFA salt. ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.38-7.18 (m, 4H), 4.54-4.42 (m, 1H), 4.28-4.14 (m, 1H), 3.93-3.70 (m, 2H), 3.19-3.00 (m, 1H), 2.75-0.69 (m, 52H); LC/MS: m/z calculated 737.4, found 738.2 (M+1)⁺.

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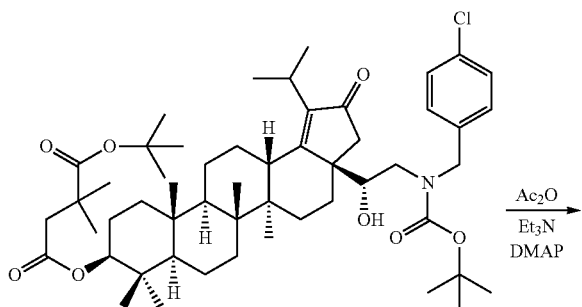
Example 15

Compound 47

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-Chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



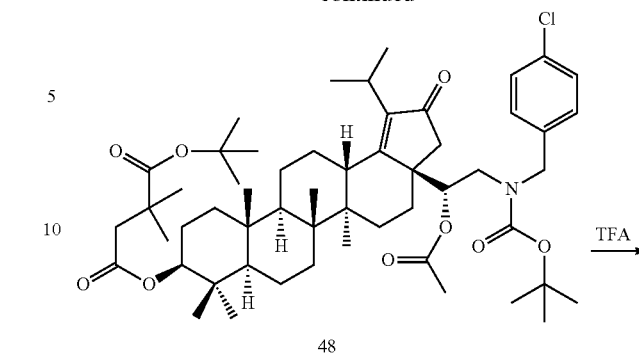
To a solution of 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate (18) (130 mg, 0.145 mmol) in DCM (30 mL) stirred at rt was added TFA (15 mL, 195 mmol). The reaction mixture was stirred at rt until LCMS and TLC indicated starting material disappeared. The solvent was evaporated and then CH₃CN and H₂O was added and the material was lyophilized to give 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-Chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (47), trifluoroacetic acid salt (120 mg, 0.139 mmol, 96% yield). ¹H NMR (400 MHz, CHLOROFORM-d) δ=10.30 (br. s., 1H), 8.08 (br. s., 1H), 7.38 (s, 4H), 4.73-4.33 (m, 2H), 4.28-4.07 (m, 2H), 3.34-3.06 (m, 2H), 2.99-2.74 (m, 2H), 2.73-2.50 (m, 2H), 2.48-2.29 (m, 1H), 2.05-0.64 (m, 47H); LC/MS: m/z calculated 737.4. found 738.3 (M+1)⁺.



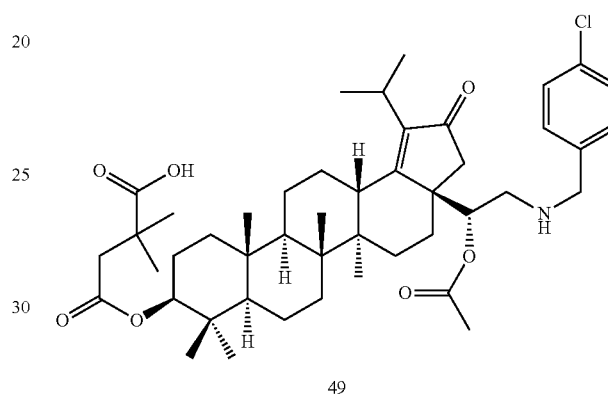
19

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-continued



47 15



49

Example 16

Compound 49

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-Acetoxy-2-((4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

55

60

65

49

135

Step A: Compound 48

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-acetoxy-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate

To a solution of 19 (500 mg, 0.559 mmol) in dichloromethane (30 mL) stirred at rt was added Ac₂O (0.158 mL, 1.677 mmol), triethylamine (0.195 mL, 1.397 mmol) and DMAP (6.83 mg, 0.056 mmol). The reaction mixture was stirred at rt until TLC indicated SM disappeared. The mixture was worked up and purified by silica gel chromatography (PE:EA=5:1) to give 48 (510 mg, 0.517 mmol, 93% yield). The product consisted of a mixture of rotomers. ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.39-7.20 (m, 2H), 7.21-6.99 (m, 2H), 5.92-5.56 (m, 1H), 5.00-3.88 (m, 2H), 3.40-1.96 (m, 8H), 1.97-0.58 (m, 67H).

Step B: Compound 49

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-Acetoxy-2-((4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

To a solution of 48 (500 mg, 0.534 mmol) in DCM (30 mL) stirred at rt was added TFA (15 mL, 195 mmol). The reaction mixture was stirred at rt until LCMS and TLC indicated SM had disappeared. The solvent was evaporated and CH₃CN and H₂O were added and mixture was lyophilized to give 49 as a trifluoroacetic acid salt (400 mg, 0.439 mmol, 82% yield). ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.46-7.19 (m, 4H), 5.94-5.70 (m, 1H), 4.58-4.36 (m, 1H), 4.25-3.88 (m, 2H), 3.25-3.02 (m, 1H), 3.01-2.41 (m, 5H), 2.08 (s, 3H), 2.00-0.64 (m, 47H);

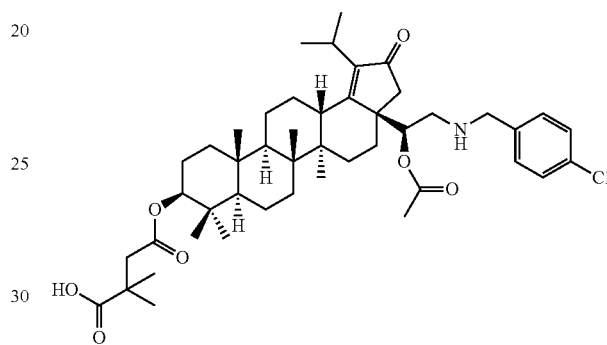
LC/MS: m/z calculated 779.5. found 780.4 (M+1)⁺.

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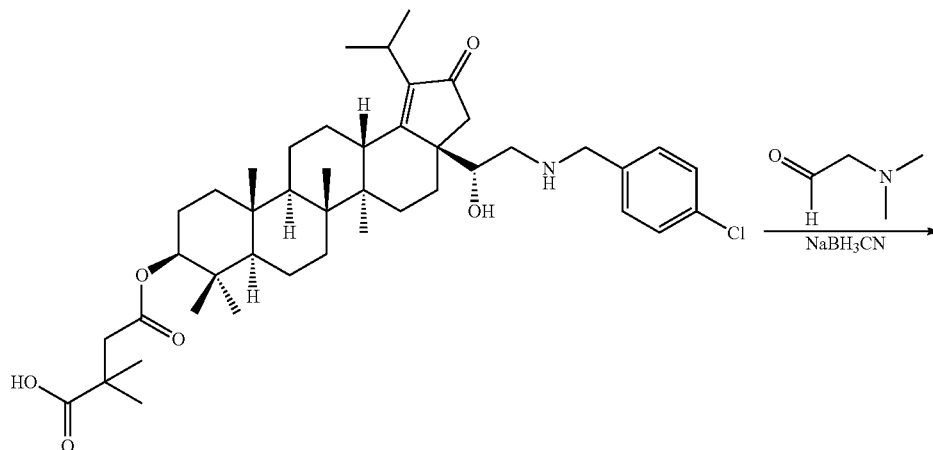
Example 17

Compound 50

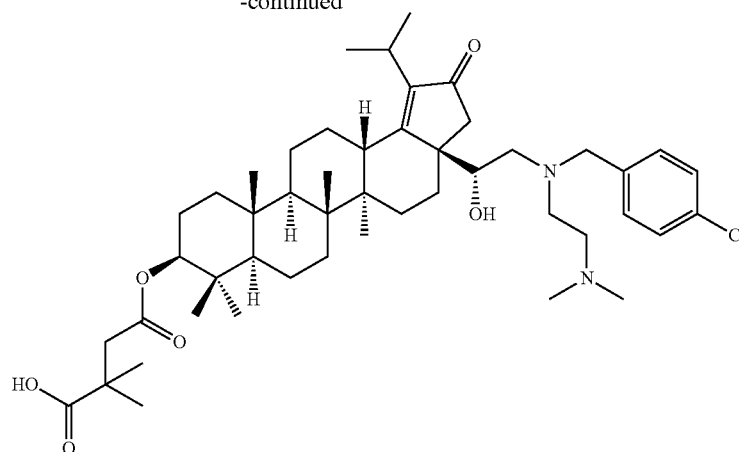
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-Acetoxy-2-((4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



The title compound was made in a similar manner to Example 16 and isolated as a TFA salt. ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.49-7.30 (m, 4H), 5.85-5.71 (m, 1H), 4.59-4.40 (m, 1H), 4.31-4.03 (m, 2H), 3.41-2.79 (m, 4H), 2.79-2.50 (m, 2H), 2.37 (d, J=18.1 Hz, 2H), 2.02-0.63 (m, 49H); LC/MS: m/z calculated 779.5. found 780.3 (M+1)⁺.



-continued

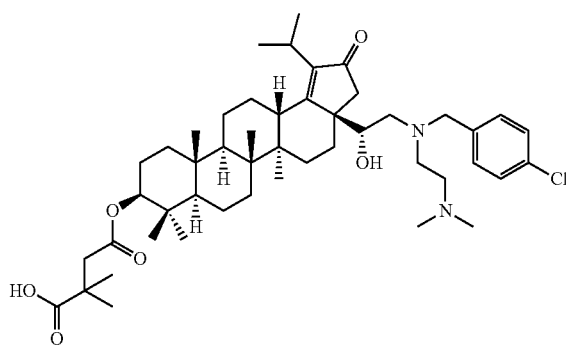


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Example 18

Compound 51

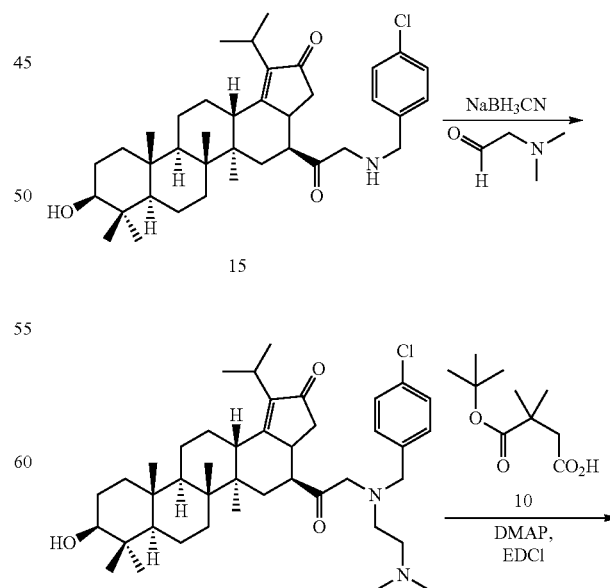
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-Chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



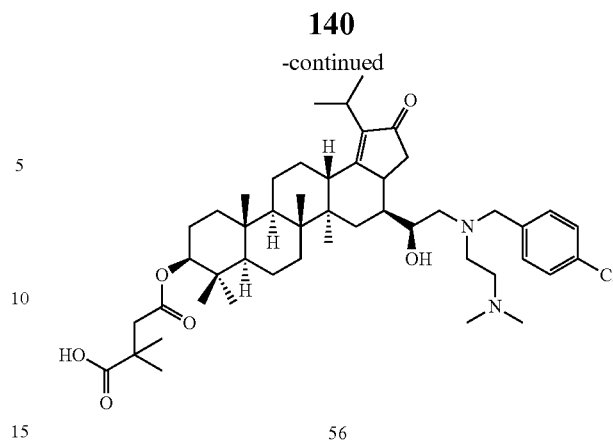
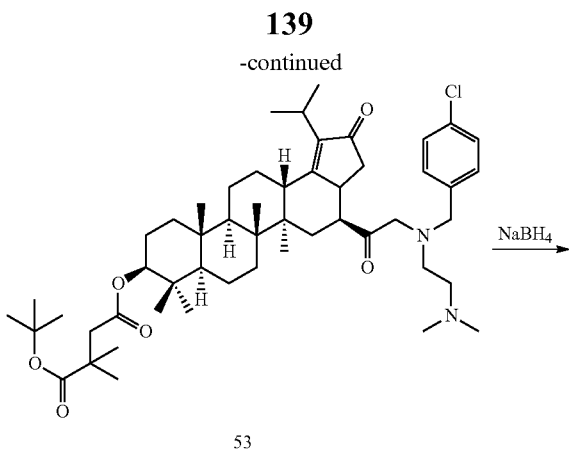
To a solution of 2-(dimethylamino)acetaldehyde, hydrochloride (6.75 g, 54.6 mmol) in methanol (20 mL) was added 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid, Trifluoroacetic acid salt (46) (9.5 g, 10.92 mmol). The pH was adjusted to 7-8 with Et₃N. The reaction mixture was stirred at rt for 2 h. Sodium cyanoborohydride (0.686 g, 10.92 mmol) was then added and the mixture was stirred at rt overnight. After the reaction was complete, water (15 mL) and EtOAc (15 mL) were added, and then the organic phase was removed and concentrated under reduced pressure. The product was extracted with EtOAc (80 mLx3), the combined organic phase was washed with brine, dried, and concentrated. The product was purified by flash chromatography (DCM:

EtOAc=2:1 to 1:1, then DCM:MeOH=100:1 to 20:1) to give 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (51) (6 g, 7.41 mmol, 67.9% yield) as white solid. Multiple batches of this material (were combined 95 g), dissolved in 600 mL of dichloromethane and washed with NaHCO₃ (400 mL*3) and the organic phase was dried over Na₂SO₄, filtered and concentrated. The solids were washed with a mixture of EtOAc: petroleum ether (600 mL), and filtered followed by lyophilization to provide the final title compound 62 g as a white solid. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.47-7.29 (m, 4H), 4.48 (dd, J=5.8, 10.3 Hz, 1H), 4.15-4.04 (m, 1H), 3.80 (d, J=13.8 Hz, 1H), 3.57 (d, J=14.1 Hz, 1H), 3.21-2.82 (m, 5H), 2.72-2.41 (m, 9H), 2.37-2.05 (m, 4H), 2.05-0.74 (m, 45H);

LC/MS: m/z calculated 808.5. found 809.5 (M+1)⁺.



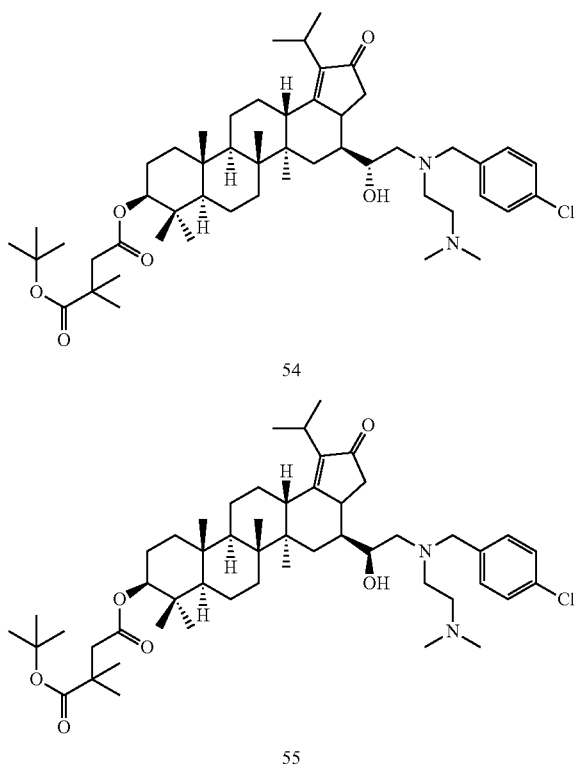
52



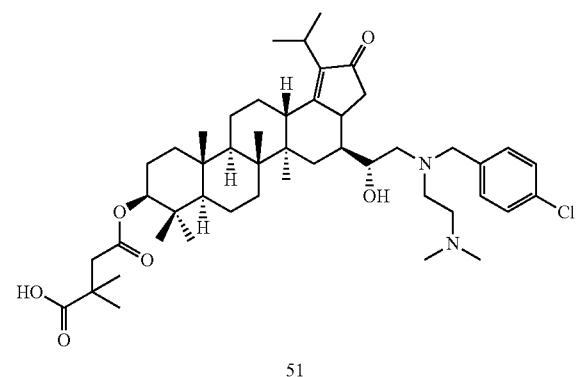
Example 19
Compound 56

4-(3aR,5aR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-Chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy-2,2-dimethyl-4-oxobutanoic acid

56



54 $\xrightarrow{\text{TFA}}$



55 $\xrightarrow{\text{TFA}}$

Step A: Compound 52

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-Chlorobenzyl)(2-(dimethylamino)ethyl)amino)acetyl)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-2-one

To a solution of 2-(dimethylamino)acetaldehyde (4.79 g, 38.8 mmol) in methanol (50 ml) and 1,2-dichloroethane (DCE) (25 ml) was added (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-(4-chlorobenzylamino)acetyl)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3a,4,5,5a,6,7,7a,8,9,10,11,11a,11b,12,13,13a-hexadecahydro-3H-cyclopenta[a]chrysen-2(5bH)-one (15) (5 g, 7.75 mmol) at 000° C. The pH was adjusted to 7 with Et₃N. The reaction mixture was stirred at rt for 1 h. Sodium cyanoborohydride (0.487 g, 7.75 mmol) was added and the mixture was stirred overnight. The reaction was diluted with water (40 ml), and extracted with DCM (60 ml×3). The combined organic layer was washed with brine (20 ml), dried over sodium sulfate and filtered to afford crude product (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)acetyl)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3a,4,5,5a,6,7,7a,8,9,10,11,11a,11b,12,13,13a-hexadecahydro-3H-cyclopenta[a]chrysen-2(5bH)-one (52) (5 g, 5.89 mmol, 76% yield) as a light yellow solid, which was used in the next step. LC/MS: m/z calculated 678.5. found 679.3 (M+1)⁺.

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Step B: Compound 53

1-Tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

To a solution of 4-(tert-butoxy)-3,3-dimethyl-4-oxobutanoic acid (11.91 g, 58.9 mmol), N,N-dimethylpyridin-4-amine (4.50 g, 36.8 mmol) in DCM (20 mL) was added EDC (11.29 g, 58.9 mmol). The reaction mixture was stirred at rt for 1 h. Then, (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)acetyl)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-2-one (52) (5 g, 7.36 mmol) was added. Upon completion, the mixture was washed with 2 M HCl, water and brine. The organic layer was dried over Na₂SO₄, filtered and concentrated to give the crude product. The product was purified by a silica gel column using dichloromethane/methanol (20:1) to afford 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (53) (1.8 g, 1.917 mmol, 26.1% yield) as an oil. ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.27 (s, 4H), 4.60-4.39 (m, 1H), 3.82 (d, J=13.8 Hz, 1H), 3.59 (d, J=13.8 Hz, 1H), 3.50-3.05 (m, 3H), 2.82-2.63 (m, 2H), 2.63-0.53 (m, 67H).

Step C: Compounds 54 and 55

1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (54) and 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (55)

To a solution of 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (53) (1.8 g, 1.917 mmol) in DCM (5 mL) was added TFA (2 mL, 26.0 mmol). The reaction mixture was stirred at rt for 1 h. The mixture was evaporated to afford the crude product. This material was purified by preparative-HPLC to provide the title compound 56 as a TFA salt (300 mg, 0.285 mmol, 68.6% yield) as a white solid. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.58-7.34 (m, 4H), 4.50 (dd, J=5.0, 11.0 Hz, 1H), 4.23-4.10 (m, 1H), 4.09-3.74 (m, 2H), 3.58-3.12 (m, 3H), 3.12-2.37 (m, 10H), 2.12-0.67 (m, 50H); LC/MS: m/z calculated 808.5. found 809.3 (M+1)⁺.

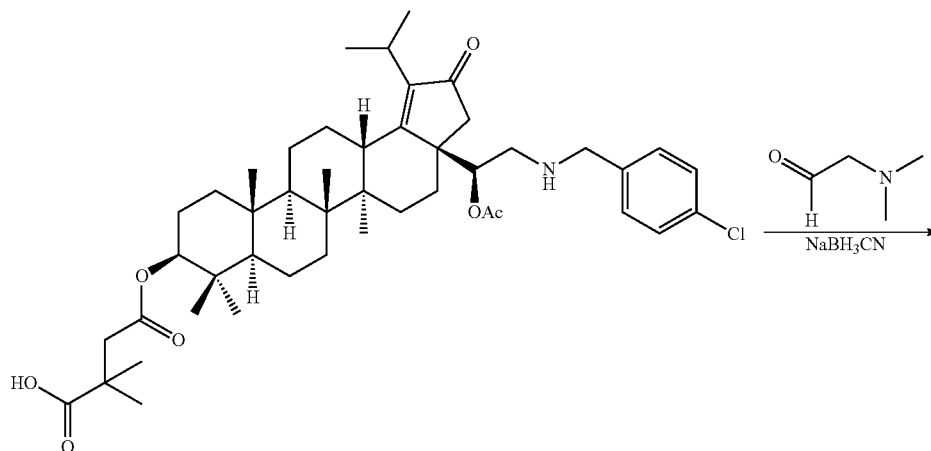
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lamino)ethyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (53) (1.5 g, 1.737 mmol) in methanol (10 mL) was added NaBH₄ (0.131 g, 3.47 mmol). The reaction mixture was stirred at rt for 1 h. The mixture then was extracted with DCM, washed with water and brine. The organic layer was dried over Na₂SO₄, and concentrated to give the crude product. This was purified by preparative-HPLC then purified by SFC to get 54 (230 mg, 15%) and 55 (360 mg 23%). For 54: ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.45-7.18 (m, 4H), 4.49 (dd, J=5.6, 10.7 Hz, 1H), 4.04 (d, J=9.8 Hz, 1H), 3.92-3.47 (m, 3H), 3.46-0.45 (m, 72H); LC/MS: m/z calculated 864.6. found 865.4 (M+1)⁺. For 55: ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.37-7.19 (m, 4H), 4.50 (dd, J=5.5, 10.5 Hz, 1H), 4.18-3.98 (m, 1H), 3.75 (d, J=13.3 Hz, 1H), 3.55 (d, J=13.3 Hz, 1H), 3.29-3.10 (m, 1H), 3.10-2.97 (m, 1H), 2.81-0.63 (m, 70H); LC/MS: m/z calculated 864.6. found 865.9 (M+1)⁺.

Step D: Compound 56

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-Chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

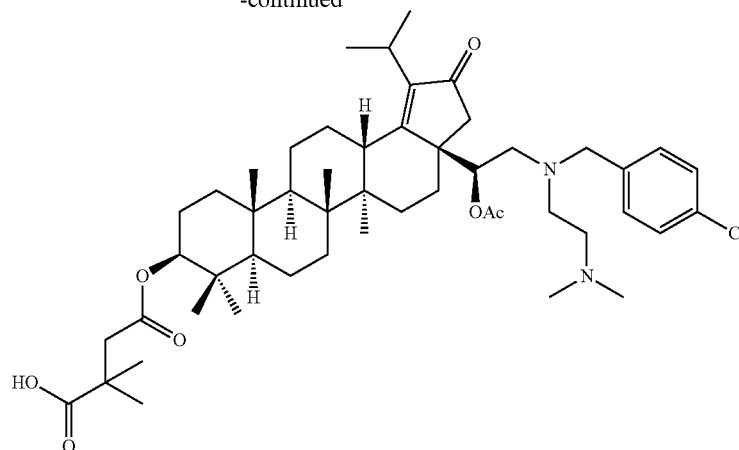
To a solution of 55 (360 mg, 0.416 mmol) in DCM (5 mL) stirred at rt was added TFA (2 mL, 26.0 mmol). The reaction mixture was stirred at rt for 1 h. The mixture was evaporated to afford the crude product. This material was purified by preparative-HPLC to provide the title compound 56 as a TFA salt (300 mg, 0.285 mmol, 68.6% yield) as a white solid. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.58-7.34 (m, 4H), 4.50 (dd, J=5.0, 11.0 Hz, 1H), 4.23-4.10 (m, 1H), 4.09-3.74 (m, 2H), 3.58-3.12 (m, 3H), 3.12-2.37 (m, 10H), 2.12-0.67 (m, 50H); LC/MS: m/z calculated 808.5. found 809.3 (M+1)⁺.



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-continued

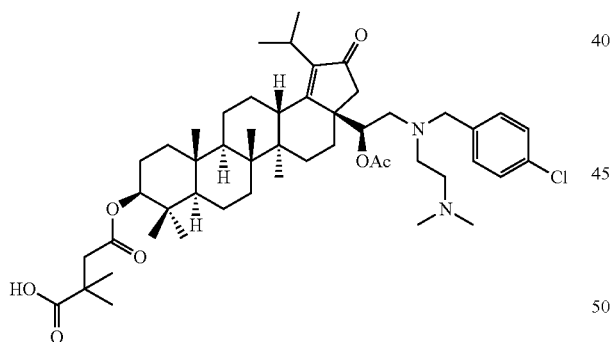


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Example 20

Compound 57

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-Acetoxy-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



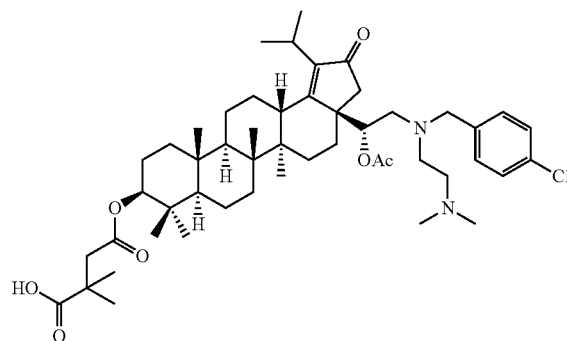
To a solution of 2-(dimethylamino)acetaldehyde, hydrochloride (238 mg, 1.922 mmol) in methanol (12 mL) was added 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (50) (150 mg, 0.192 mmol). The reaction mixture was stirred at rt for 2 h then sodium cyanoborohydride (121 mg, 1.922 mmol) was added and the mixture was stirred overnight. Upon completion, the mixture was purified preparative-HPLC to provide the title compound (50 mg, 24%). ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.35-7.12 (m, 4H), 5.65 (d, J=9.3 Hz, 1H), 4.49 (dd, J=5.8, 10.0 Hz, 1H), 3.83 (d, J=13.6 Hz, 1H), 3.55 (d, J=13.6 Hz, 1H), 3.25-2.91 (m, 7H), 2.91-

2.73 (m, 7H), 2.73-2.52 (m, 3H), 2.33 (d, J=18.1 Hz, 1H), 1.99-0.72 (m, 48H); LC/MS: m/z calculated 850.5. found 851.4 (M+1)⁺.

Example 21

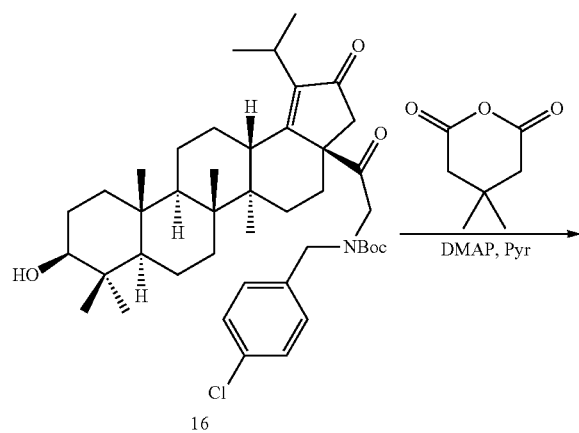
Compound 58

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-Acetoxy-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



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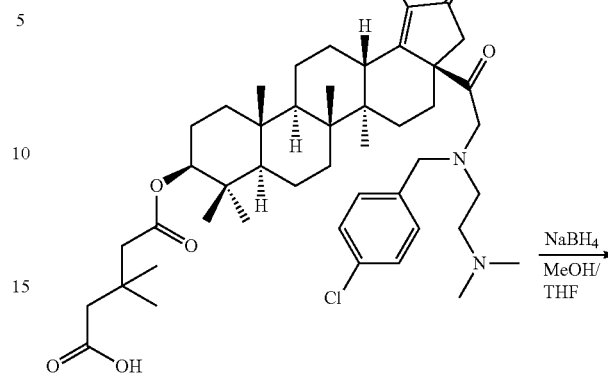
The title compound was made in a similar manner to example 20. ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.40-7.10 (m, 4H), 5.68 (d, J=9.8 Hz, 1H), 4.55-4.39 (m, 1H), 3.81 (d, J=13.8 Hz, 1H), 3.57 (d, J=13.8 Hz, 1H), 3.29-2.74 (m, 11H), 2.74-2.27 (m, 6H), 2.14 (s, 3H), 2.09-0.68 (m, 46H); LC/MS: m/z calculated 850.5. found 851.4 (M+1)⁺.

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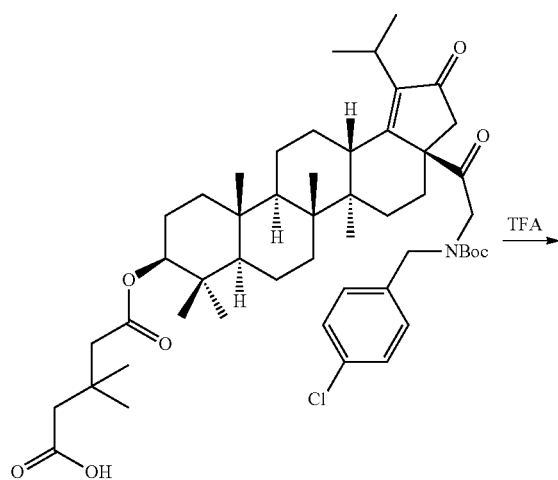
16

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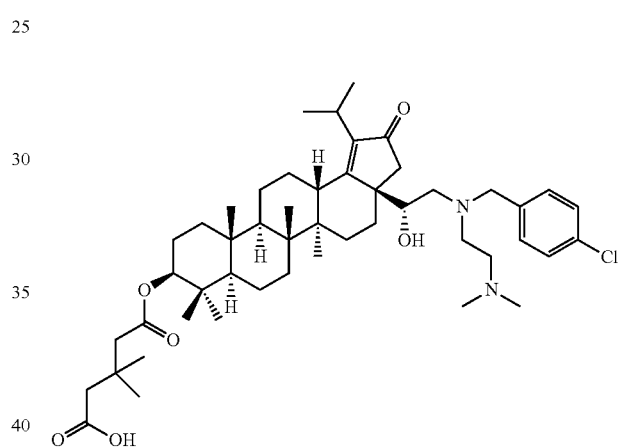
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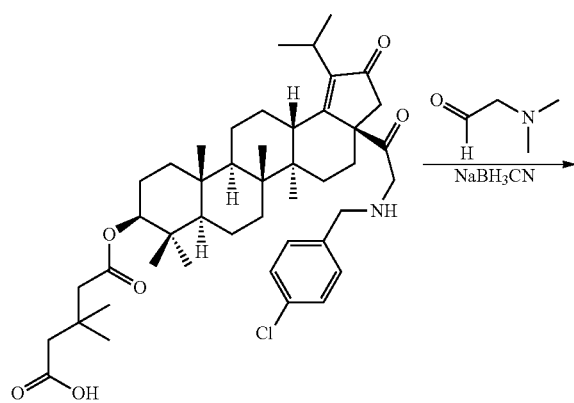
61



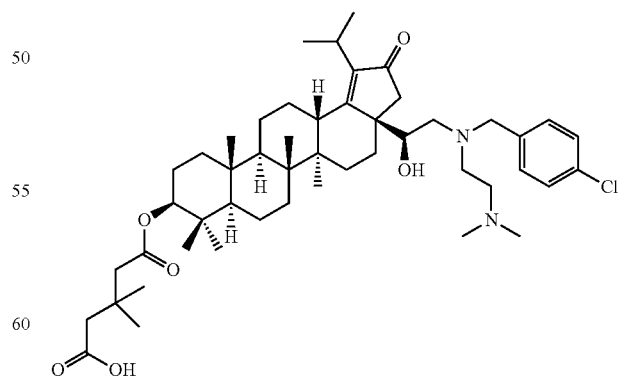
59



62



60



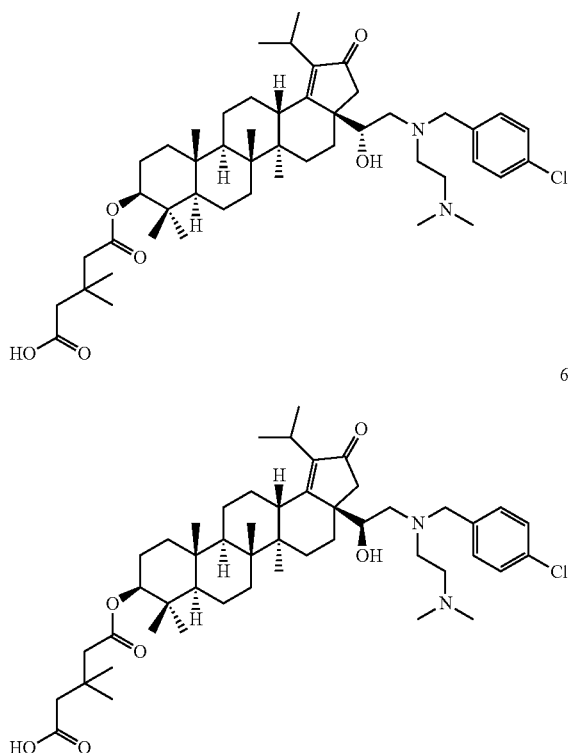
63

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Example 22 and 23

Compound 62 and 63

5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-Chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid (62) and 5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-Chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid (63)



Step A: Compound 59

5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid

To a solution of tert-butyl 4-chlorobenzyl(2-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-oxoethyl)carbamate (15) (1 g, 1.412 mmol), DMAP (0.517 g, 4.23 mmol) in pyridine (2 ml) stirred

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at rt was added 4,4-dimethyl-dihydro-3H-pyran-2,6-dione (1.003 g, 7.06 mmol). The reaction mixture was stirred at 50° C. for 5 h. The mixture was diluted with EtOAc and washed with water. The resultant extract was purified by silica gel column to provide 59 (800 mg, 60%). ¹H NMR (500 MHz, CHLOROFORM-d) δ=8.67 (br. s., 1H), 7.98-7.36 (m, 1H), 7.33-7.27 (m, 2H), 7.21-7.09 (m, 2H), 4.62-4.26 (m, 3H), 4.07-3.42 (m, 2H), 3.30-3.05 (m, 1H), 2.66-0.66 (m, 61H).

Step B: Compound 60

5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-Chlorobenzyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid

To a solution of 5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid (59) (800 mg, 0.941 mmol) in dichloromethane (6 mL) stirred at rt was added trifluoroacetic acid (2 mL, 0.941 mmol). The reaction mixture was stirred at rt for 1 h. The mixture was evaporated to provide the target compound (600 mg, 81%) which was used without further purification. LC/MS: m/z calculated 749.4. found 750.1 (M+1)⁺.

Step C: Compound 61

5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-Chlorobenzyl)(2-(dimethylamino)ethyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid

To a solution of 5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-chlorobenzyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid, trifluoroacetic acid salt (60) (700 mg, 0.810 mmol) in methanol (30 mL) was added 2-(dimethylamino)acetaldehyde (353 mg, 4.05 mmol) at 000° C. The pH was adjusted to 7 with Et₃N. The reaction mixture was stirred at rt for 1 h and sodium cyanoborohydride (50.9 mg, 0.810 mmol) was added and the resultant mixture was stirred overnight. The reaction was diluted with water (40 mL) and extracted with DCM (60 mL×3). The combined organic layer was washed with brine (20 mL), dried over sodium sulfate and filtered to afford crude product 5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid, trifluoroacetic acid salt (61) (200 mg, 23% yield) as a light yellow solid. ¹H NMR (500 MHz, METHANOL-d₄) δ=7.39 (s, 4H), 4.49 (dd, J=5.7, 10.7 Hz, 1H), 3.95 (d, J=13.6 Hz, 1H), 3.57 (d, J=13.2 Hz, 1H), 3.40-3.29 (m, 1H), 3.27-3.16 (m, 2H), 3.05 (s, 6H), 3.00-2.88 (m, 2H), 2.57-2.26 (m, 6H), 2.09 (d, J=19.5 Hz, 1H), 2.04-0.75 (m, 47H); LC/MS: m/z calculated 820.5. found 821.3 (M+1)⁺.

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Step D: Compounds 62 and 63

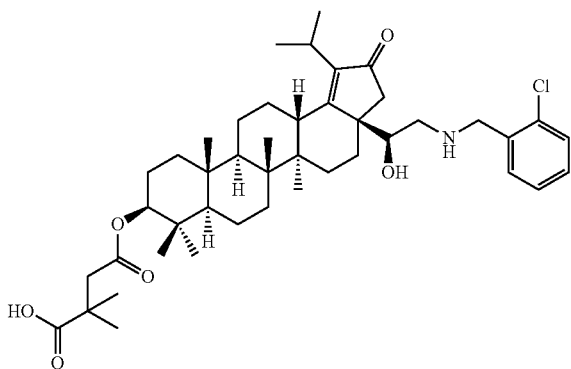
5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)(isopentyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid (62) and 5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)(isopentyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid (63)

To a solution of 5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid, trifluoroacetic acid salt (61) (140 mg, 0.133 mmol) in methanol (10 mL) stirred at 0° C. was added NaBH₄ (10.09 mg, 0.267 mmol). The reaction mixture was stirred at 0° C. for 1 h, then more NaBH₄ (10.09 mg, 0.267 mmol) was added. After an additional 1 h at 000° C., the mixture was warmed to rt stirred for another 1 h. LCMS indicated the reaction was complete. EtOAc was added and the mixture was washed with water. The organic phase was evaporated to give the crude which was purified by preparative-HPL to give two diastereomers. 5 mg of isomer A (62) was isolated (3.5% yield) and 10 mg of isomer B (63) was isolated (7%). The stereochemistry of the newly formed stereocenter in each isomer was assigned by spectral similarity to compounds 51 (analogous to 62) and 56 (analogous to 63). For isomer A (62): ¹H NMR (500 MHz, METHANOL-d₄) δ=7.48-7.30 (m, 4H), 4.57-4.43 (m, 1H), 4.14 (d, J=10.1 Hz, 1H), 3.91-3.74 (m, 1H), 3.67 (d, J=13.9 Hz, 1H), 3.26-3.10 (m, 2H), 3.10-2.93 (m, 2H), 2.93-2.81 (m, 6H), 2.68-2.10 (m, 9H), 2.06-0.65 (m, 46H); LC/MS: m/z calculated 822.5. found 823.5 (M+1)⁺. For isomer B (63): ¹H NMR (500 MHz, METHANOL-d₄) δ=7.43 (br. s., 4H), 4.51 (dd, J=5.8, 9.9 Hz, 1H), 4.16 (d, J=10.1 Hz, 1H), 3.98-3.75 (m, 2H), 3.52-3.37 (m, 1H), 3.31-3.02 (m, 3H), 3.02-2.71 (m, 9H), 2.64-2.34 (m, 6H), 2.19-0.69 (m, 46H); LC/MS: m/z calculated 822.5. found 823.4 (M+1)⁺.

Example 24

Compound 64

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((2-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



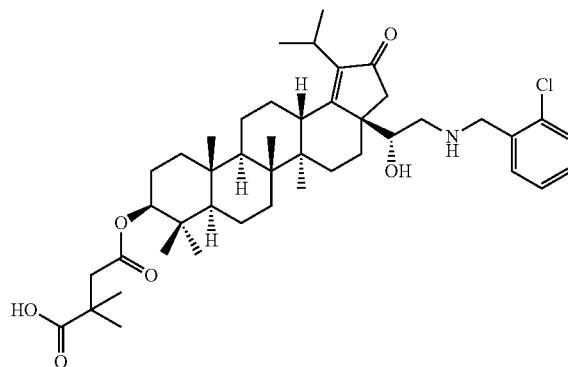
150

The title compound was made in a similar manner to example 14. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.73-7.38 (m, 4H), 4.65-4.37 (m, 4H), 3.44 (d, J=12.3 Hz, 1H), 3.39-3.22 (m, 1H), 3.11-2.96 (m, 2H), 2.62 (q, J=16.0 Hz, 2H), 2.48 (d, J=18.3 Hz, 1H), 2.21-0.77 (m, 46H); LC/MS: m/z calculated 737.4. found 738.3 (M+1)⁺.

Example 25

Compound 65

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

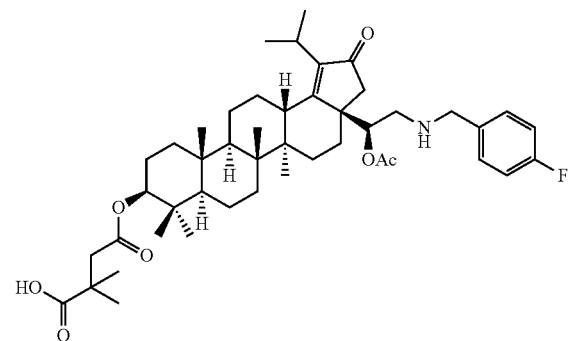


The title compound was made in a similar manner to example 14. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.63-7.37 (m, 4H), 4.55-4.31 (m, 4H), 3.26-3.11 (m, 1H), 3.01-2.46 (m, 6H), 2.36-2.16 (m, 1H), 2.15-0.79 (m, 45H); LC/MS: m/z calculated 737.4. found 738.0 (M+1)⁺.

Example 26

Compound 66

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-Acetoxy-2-((4-fluorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



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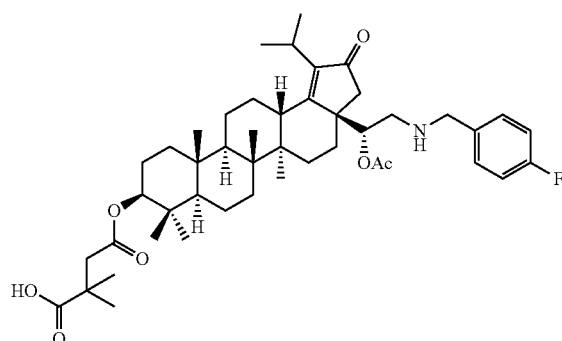
The title compound was made as a TFA salt in a similar manner to example 16. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically.

¹H NMR (400 MHz, CHLOROFORM-d) δ=10.54-8.79 (m, 1H), 7.50-7.34 (m, 2H), 7.19-6.99 (m, 2H), 5.81 (d, J=9.8 Hz, 1H), 4.49 (dd, J=5.8, 10.3 Hz, 1H), 4.31-3.93 (m, 2H), 3.26 (d, J=12.5 Hz, 1H), 3.20-3.05 (m, 1H), 3.05-2.82 (m, 2H), 2.80-2.47 (m, 2H), 2.36 (d, J=18.1 Hz, 1H), 2.05-0.57 (m, 49H); LC/MS: m/z calculated 763.5. found 764.3 (M+1)⁺.

Example 27

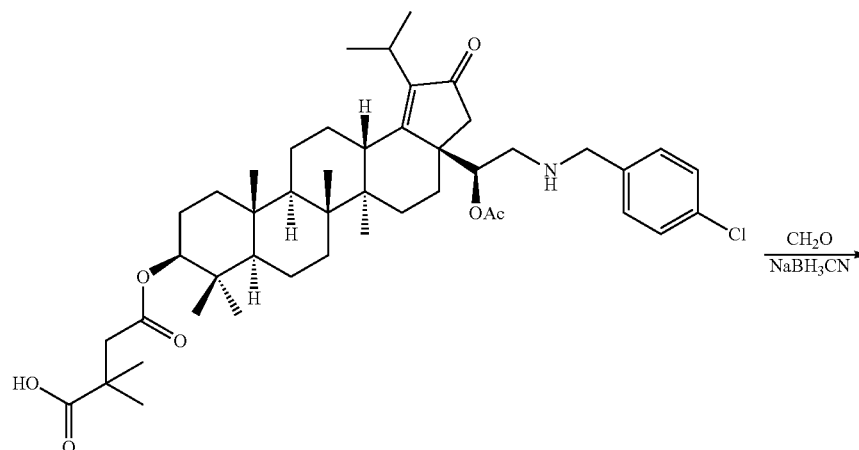
Compound 67

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-acetoxy-2-((4-fluorobenzyl)amino)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



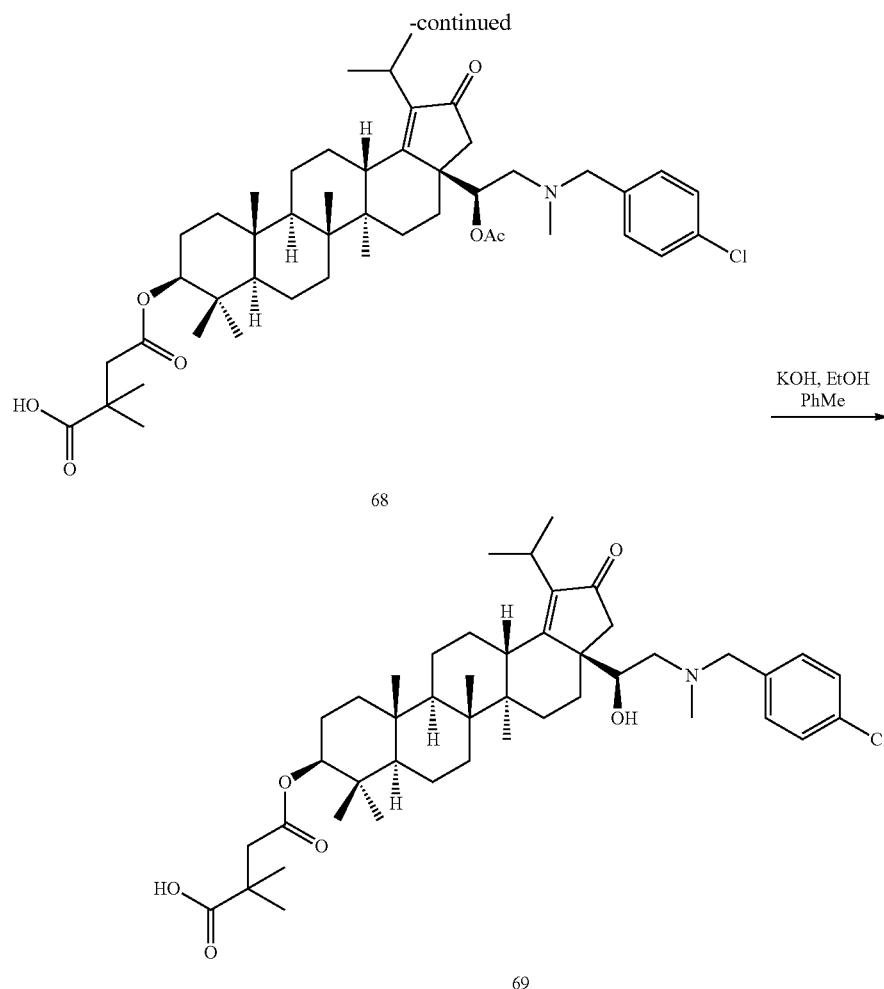
The title compound was made as a TFA salt in a similar manner to example 16. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically.

¹H NMR (400 MHz, CHLOROFORM-d) δ=9.65 (br. s., 1H), 7.46-7.28 (m, 2H), 7.03 (t, J=8.2 Hz, 2H), 5.86 (br. s., 1H), 4.50 (dd, J=5.5, 10.3 Hz, 1H), 4.29-4.06 (m, 1H), 4.06-3.85 (m, 1H), 3.19-2.99 (m, 1H), 2.81-2.39 (m, 6H), 2.21-0.62 (m, 49H); LC/MS: m/z calculated 763.5. found 764.3 (M+1)⁺.



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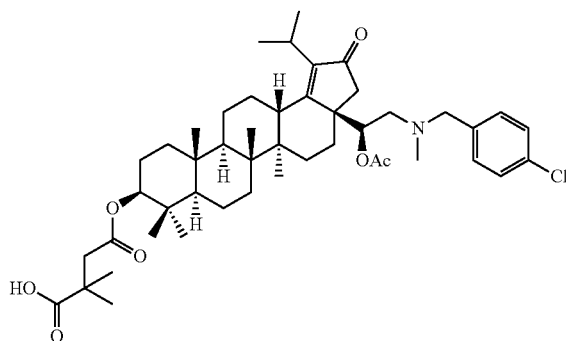
154



Example 28

Compound 68

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((4-fluorobenzyl)(methyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



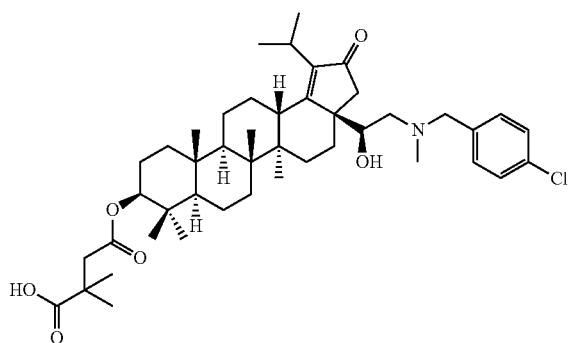
To a solution of 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (50) (150 mg, 0.192 mmol) in MeOH (6 mL) stirred in air at rt was added formaldehyde (31.2 mg, 0.384 mmol). The reaction mixture was stirred at rt for 2 h. Then it was added NaCNBH₃ (85 mg, 1.345 mmol) portionwise and stirred for overnight. The solvent was evaporated and the residue diluted with DCM and washed with water and brine. The dried organics were filtered and concentrated to give 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((4-chlorobenzyl)(methyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (68) (120 mg, 65% yield) as a white solid. This material was used without further purification. ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.31-7.26 (m, 2H), 7.24-7.16 (m, 2H), 5.65 (d, J=8.5 Hz, 1H), 4.50 (br. s., 1H), 3.66-3.51 (m, 1H), 3.49-3.36 (m, 1H), 3.27-3.06 (m, 2H), 2.73-2.32 (m, 5H), 2.26 (s, 3H), 2.08-0.73 (m, 49H); LC/MS: m/z calculated 793.5. found 794.3 (M+1)⁺.

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Example 29

Compound 69

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-Chlorobenzyl)(methyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



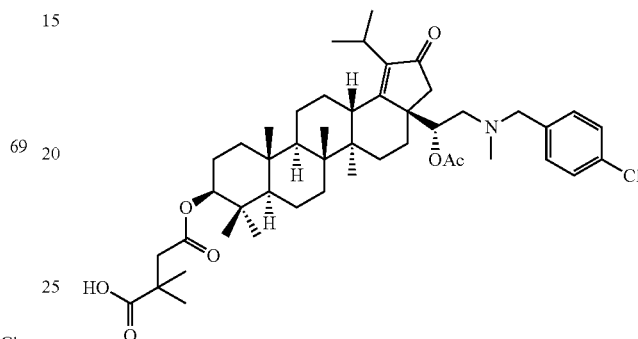
To a solution of 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((4-chlorobenzyl)(methyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (68) (120 mg, 0.151 mmol) in ethanol (2 mL) and toluene (2 mL) was added potassium hydroxide (15.25 mg, 0.272 mmol). The reaction mixture was stirred at rt for 30 min. The reaction mixture was neutralized with aqueous 1N HCl to pH=7 and evaporated to obtain the residue. This was extracted with DCM, washed with water and dried to yield the crude product which was purified by preparative-HPLC to afford 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)(methyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid as a trifluoroacetate salt (95 mg, 72% yield) as a white solid. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.55 (s, 4H), 4.60-4.12 (m, 3H), 3.32-3.19 (m, 1H), 3.18-2.84 (m, 5H), 2.71-2.52 (m, 2H), 2.11-0.78 (m, 49H); LC/MS: m/z calculated 751.5. found 752.4 (M+1)⁺.

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Example 30

Compound 70

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-Acetoxy-2-((4-chlorobenzyl)(methyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

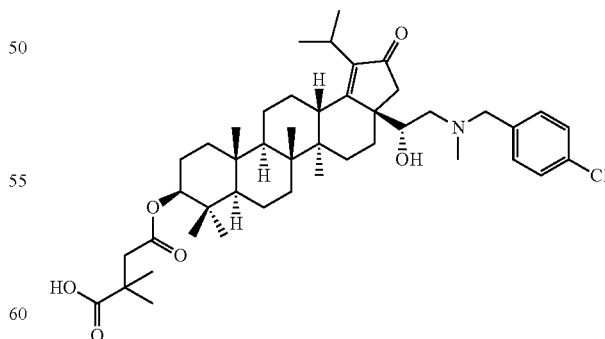


The title compound was made in similar manner to example 28. ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.31-7.23 (m, 2H), 7.22-7.13 (m, 2H), 5.66 (dd, J=2.4, 8.7 Hz, 1H), 4.55-4.43 (m, 1H), 3.51-3.35 (m, 2H), 3.19-3.05 (m, 1H), 2.74-2.42 (m, 5H), 2.42-0.66 (m, 53H); LC/MS: m/z calculated 793.5. found 794.5 (M+1)⁺.

Example 31

Compound 71

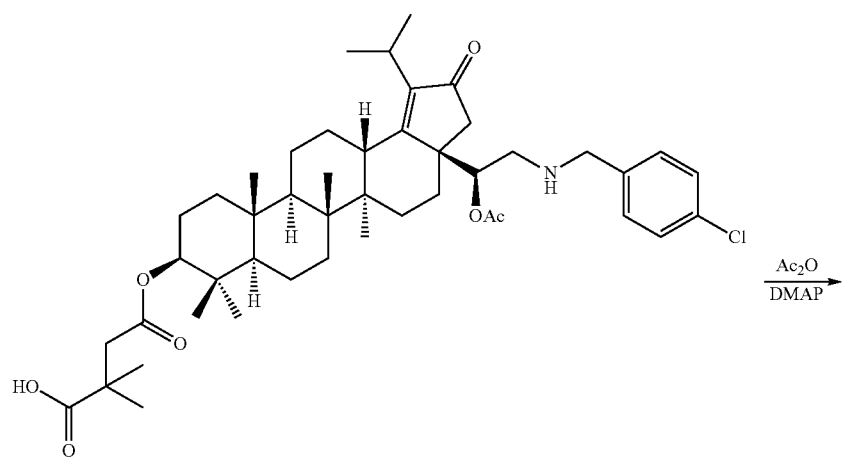
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-Chlorobenzyl)(methyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



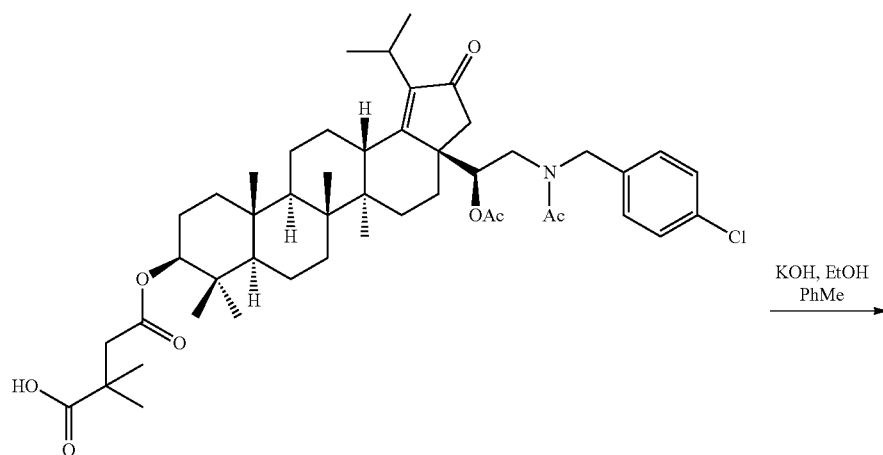
The title compound was made in similar manner to example 29. ¹H NMR (500 MHz, METHANOL-d₄) δ=7.63-7.38 (m, 4H), 4.56-4.25 (m, 4H), 3.25-3.14 (m, 1H), 2.99 (s, 3H), 2.82-2.52 (m, 4H), 2.52-2.32 (m, 2H), 2.24 (d, J=12.9 Hz, 1H), 2.09-0.77 (m, 45H); LC/MS: m/z calculated 751.5. found 752.3 (M+1)⁺.

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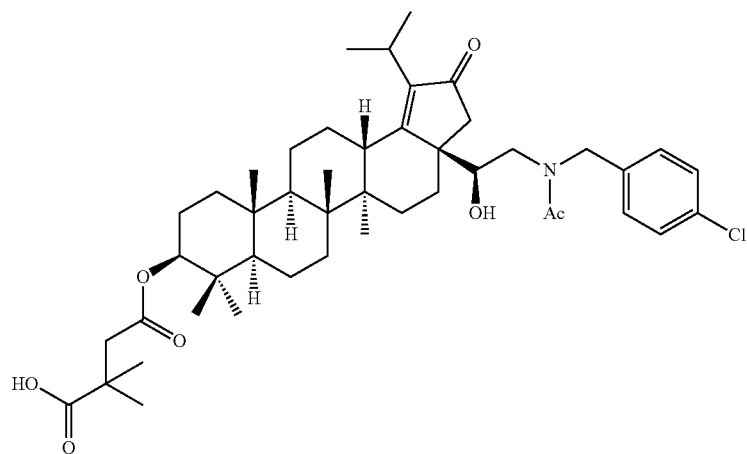
158



50



72



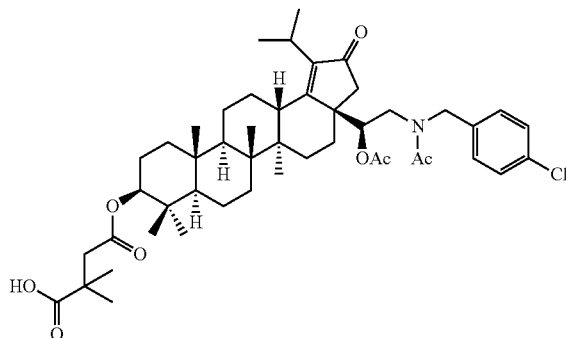
73

159

Example 32

Compound 72

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-Acetoxy-2-(N-(4-chlorobenzyl)acetamido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



A mixture of 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-(N-(4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (50) (200 mg, 0.256 mmol), TEA (0.332 mL, 2.56 mmol), DMAP (6.3 mg, 0.05 mmol) and in DCM (5 mL) was stirred for 3 h. The mixture was quenched with water (50 mL), washed with water (2x50 mL), dried over Na₂SO₄, filtered and concentrated in vacuo to afford 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-(N-(4-chlorobenzyl)acetamido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (72) (160 mg, 0.182 mmol, 71.0% yield) as a white solid. ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.42-7.24 (m, 2H), 7.24-6.90 (m, 2H), 5.98-5.68 (m, 1H), 5.15-4.56 (m, 1H), 4.56-4.45 (m, 1H), 4.40-3.98 (m, 2H), 2.29-0.68 (m, 66H), 3.48-0.58 (m, 58H);

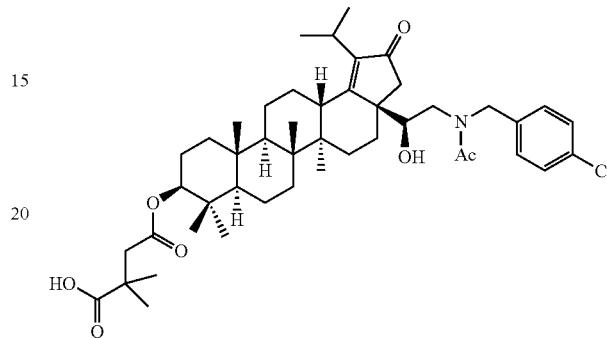
LC/MS: m/z calculated 821.5. found 822.3 (M+1)⁺.

160

Example 33

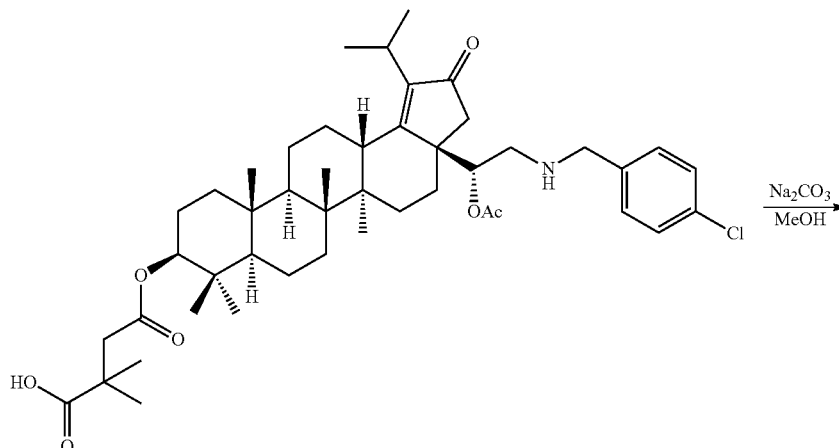
Compound 73

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(N-(4-Chlorobenzyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



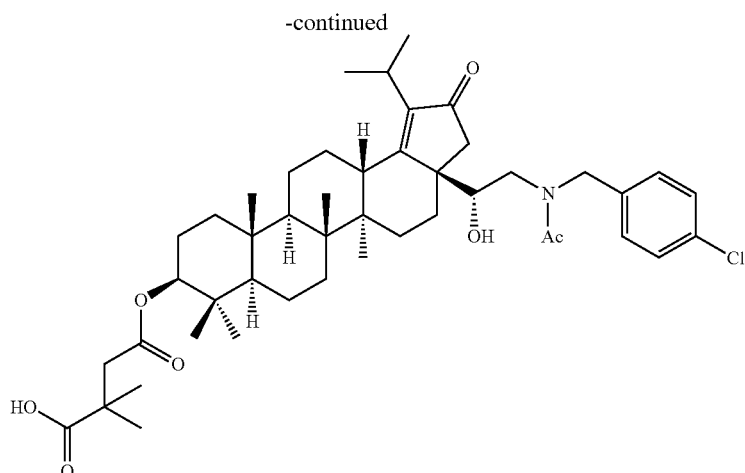
To a solution of 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-(N-(4-chlorobenzyl)acetamido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (72) (150 mg, 0.182 mmol) in ethanol (2 mL) and toluene (2 mL) was added potassium hydroxide (40.9 mg, 0.729 mmol). The reaction mixture was stirred at rt for min. The reaction mixture was neutralized with aqueous 1 N HCl to pH=7 and concentrated to obtain a residue. The residue was extracted with DCM, washed with water and dried to yield the crude product which was purified by preparative-HPLC to afford 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(N-(4-chlorobenzyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (73) (40 mg, 28%) as a white solid. Compound exists as a mixture of rotomers; ¹H NMR (400 MHz, DMSO-d₆) δ=12.18 (br. s., 1H), 7.52-7.14 (m, 4H), 5.03-3.77 (m, 5H), 3.39-2.80 (m, 3H), 2.62-2.54 (m, 1H), 2.27 (t, J=17.2 Hz, 1H), 2.20-0.58 (m, 51H);

LC/MS: m/z calculated 779.5. found 802.3 (M+Na)⁺.



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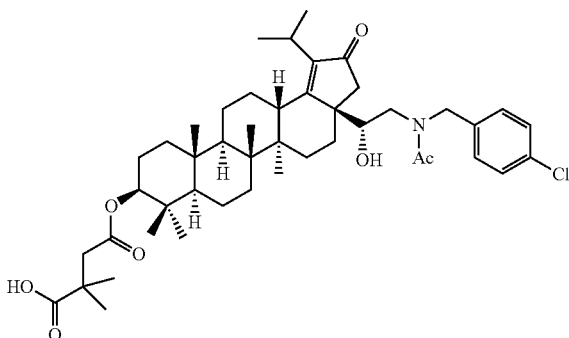
162



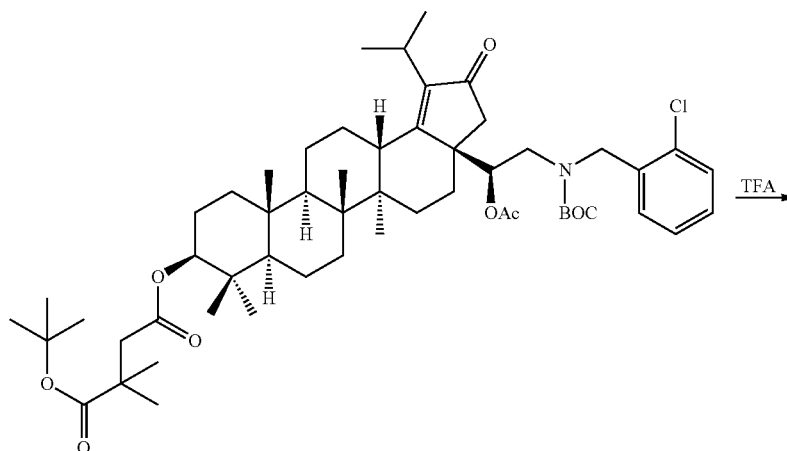
74

Example 34
Compound 74

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(4-Chlorobenzyl)acetamido)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



A mixture of 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,
13aS)-3a-((R)-1-acetoxy-2-((4-chlorobenzyl)amino)ethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid (49) (150 mg, 0.192 mmol), Na₂CO₃ (20.37
mg, 0.192 mmol), in methanol (3 mL) was stirred for 3 h, then
purified by preparative-HPLC to afford 4-(((3aR,5aR,5bR,
7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(N-(4-chlorobenzyl)
acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid (74) (45 mg, 30%) as
a white solid. Compound exists as a mixture of rotomers; ¹H
NMR (500 MHz, METHANOL-d₄) δ=7.43-7.27 (m, 2H),
7.28-7.11 (m, 2H), 5.30-4.09 (m, 6H), 3.55-2.09 (m, 11H),
2.09-0.78 (m, 44H); LC/MS: m/z calculated 779.5. found
780.4 (M+1)⁺.

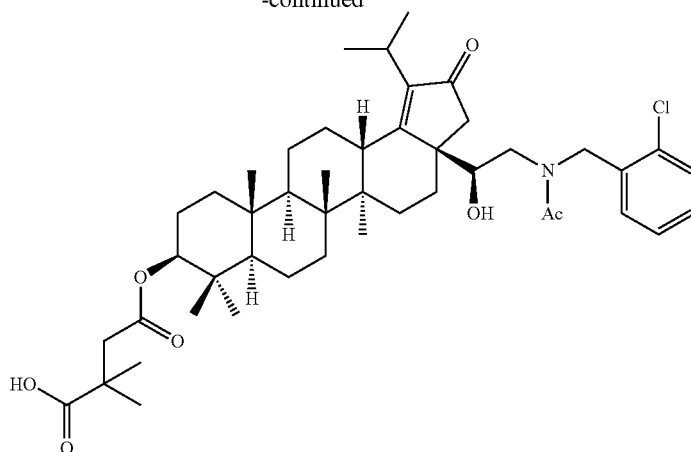


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-continued



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Example 35

Compound 76

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(N-(2-Chlorobenzyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

Stereochemistry was tentatively assigned as drawn, but not fully confirmed spectroscopically. The compound exists as a mixture of rotomers. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.55-7.14 (m, 4H), 5.10-4.72 (m, 2H), 4.72-3.97 (m, 3H), 3.54-3.39 (m, 1H), 3.30-3.21 (m, 1H), 3.13-2.97 (m, 1H), 2.84-0.69 (m, 53H);

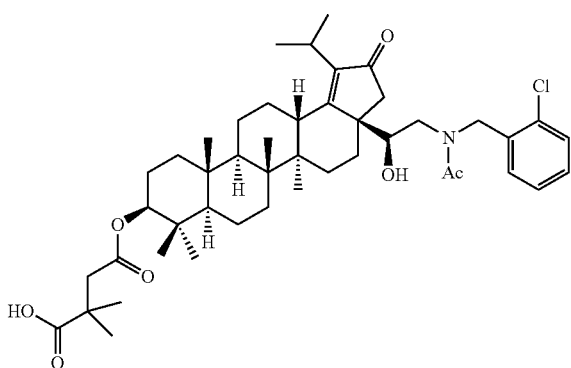
LC/MS: m/z calculated 779.5. found 780.3 (M+1)⁺.

Example 36

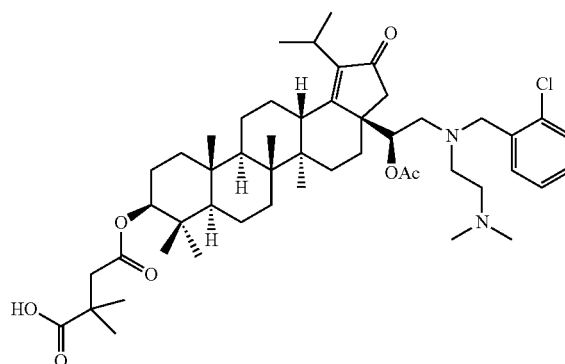
Compound 77

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-Acetoxy-2-((2-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

77



To a solution of 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((tert-butoxycarbonyl)(2-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate (75, made in a similar manner to compound 48) (100 mg, 0.107 mmol) in DCM (30 mL) stirred at rt was added TFA (15 mL, 195 mmol). The reaction mixture was stirred at rt until LCMS and TLC indicated SM disappeared. The solvent was removed to give the crude product purified by preparative HPLC to give 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(N-(2-chlorobenzyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (40 mg, 48%).



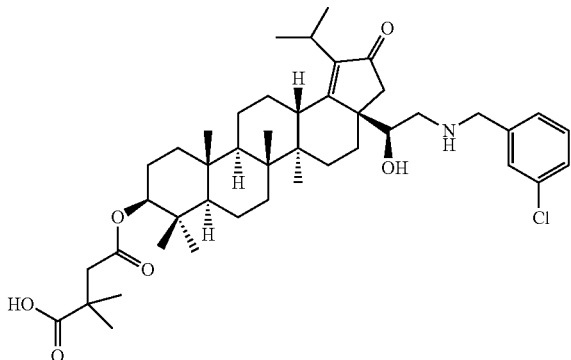
The title compound was made in a similar manner to Example 20. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, CHLOROFORM-d) δ=7.64-7.06 (m, 4H), 5.61 (d, J=8.8 Hz, 1H), 4.50 (dd, J=5.4, 10.7 Hz, 1H), 3.82 (d, J=13.8 Hz, 1H), 3.65 (d, J=13.6 Hz, 1H), 3.26-2.92 (m, 7H), 2.89-2.74 (m, 7H), 2.74-2.53 (m, 3H), 2.26 (d, J=18.3 Hz, 1H), 1.93-0.67 (m, 48H); LC/MS: m/z calculated 850.5. found 851.4 (M+1)⁺.

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Example 37

Compound 78

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((3-Chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

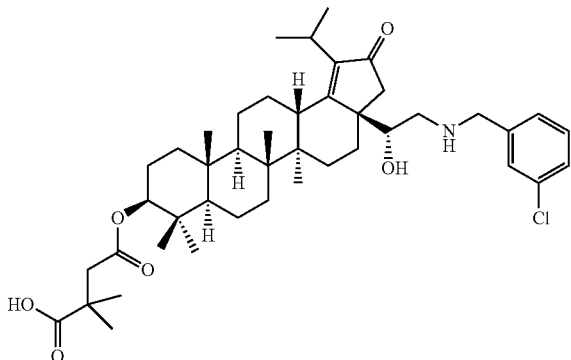


The title compound was made in a similar manner to example 20 as a TFA salt. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.61 (s, 1H), 7.56-7.43 (m, 3H), 4.57-4.44 (m, 2H), 4.35-4.21 (m, 2H), 3.38 (dd, J=2.5, 12.5 Hz, 1H), 3.31-3.23 (m, 1H), 3.09-3.01 (m, 1H), 2.96 (t, J=11.8 Hz, 1H), 2.71-2.51 (m, 1H), 2.46 (d, J=18.3 Hz, 1H), 2.15-0.79 (m, 48H); LC/MS: m/z calculated 737.4. found 738.3 (M+1)⁺.

Example 38

Compound 79

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((3-Chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



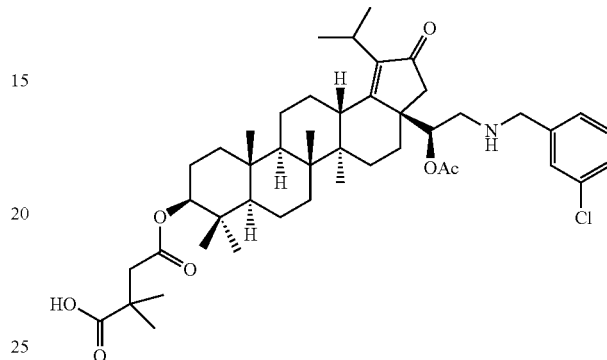
The title compound was made in a similar manner to example 20 as a TFA salt. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.77-7.28 (m, 4H), 4.68-4.15 (m, 4H), 3.27-3.11 (m, 1H), 2.73-2.48 (m, 5H), 2.38-2.17 (m, 1H), 2.16-0.71 (m, 4H); LC/MS: m/z calculated 737.4. found 738.4 (M+1)⁺.

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Example 39

Compound 80

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-Acetoxy-2-((3-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

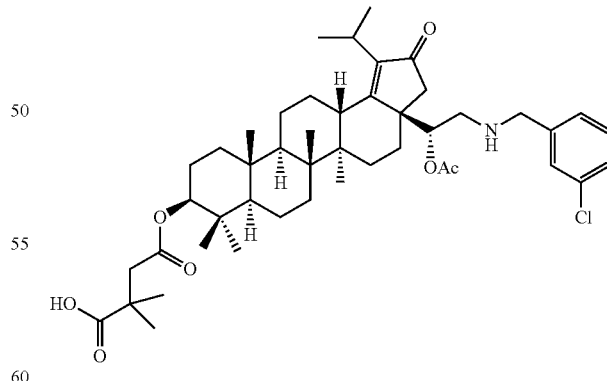


The title compound was made in a similar manner to example 16 as a TFA salt. Stereochemistry was tentatively assigned as drawn, but not fully confirmed spectroscopically. ¹H NMR (500 MHz, CHLOROFORM-d) δ=7.43 (s, 1H), 7.42-7.32 (m, 3H), 5.81 (d, J=10.1 Hz, 1H), 4.49 (dd, J=5.5, 10.2 Hz, 1H), 4.24 (d, J=13.2 Hz, 1H), 4.13-3.96 (m, 1H), 3.34-3.04 (m, 2H), 3.05-2.82 (m, 2H), 2.75-2.62 (m, 1H), 2.62-2.52 (m, 1H), 2.37 (d, J=18.0 Hz, 1H), 1.93 (s, 3H), 1.90-0.65 (m, 47H); LC/MS: m/z calculated 779.5. found 780.3 (M+1)⁺.

Example 40

Compound 81

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-Acetoxy-2-((3-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



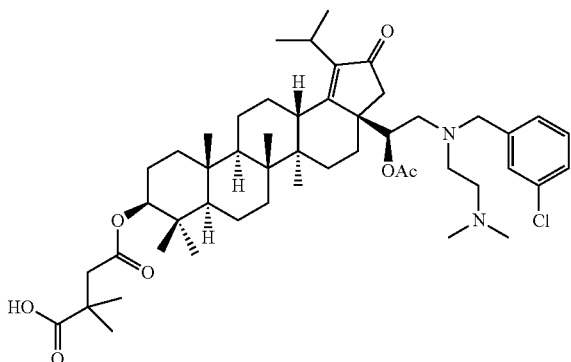
The title compound was made in a similar manner to Example 16 as a TFA salt. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (500 MHz, CHLOROFORM-d) δ=9.77 (br. s., 1H), 7.50-7.09 (m, 4H), 5.87 (br. s., 1H), 4.57-4.44 (m, 1H), 4.12 (d, J=1.6 Hz, 1H), 3.96 (d, J=13.2 Hz, 1H), 3.23-3.00 (m, 1H), 2.86-2.37 (m, 5H), 2.20-0.66 (m, 50H); LC/MS: m/z calculated 779.5. found 780.2 (M+1)⁺.

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Example 41

Compound 82

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((3-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



82

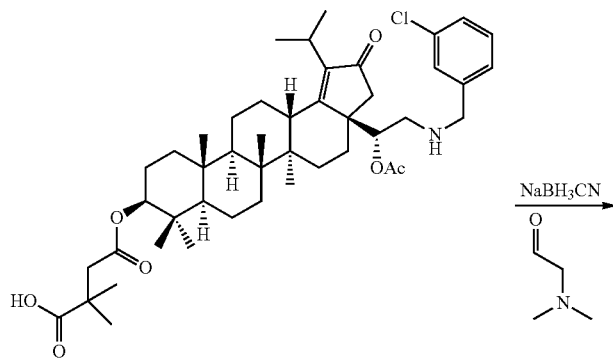
10

15

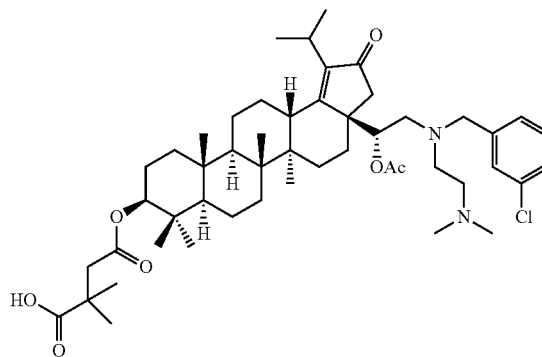
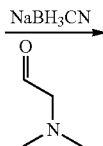
20

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The title compound was made in a similar manner to Example 18 as a TFA salt. To a solution of 2-(dimethylamino) acetaldehyde (553 mg, 4.47 mmol) in methanol (10 ml), was added 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((3-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid, trifluoroacetic acid salt (80) (400 mg, 0.447 mmol). The reaction mixture was stirred at 40° C. for 2 h. The reaction was cooled to rt and NaBH₃CN (281 mg, 4.47 mmol) was added. The mixture and stirred overnight. Then concentrated in vacuo and purified by preparative-HPLC to afford 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((3-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (82) (80 mg, 20%) as a light yellow solid. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 850.5. found 851.5 (M+1)⁺.

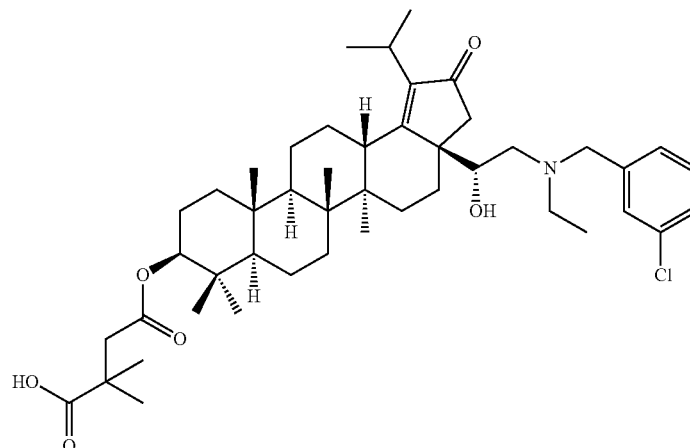


81



83

+



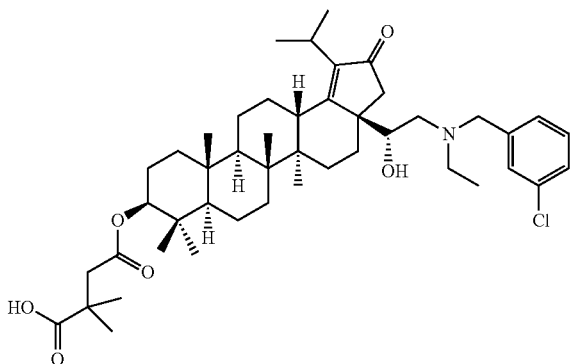
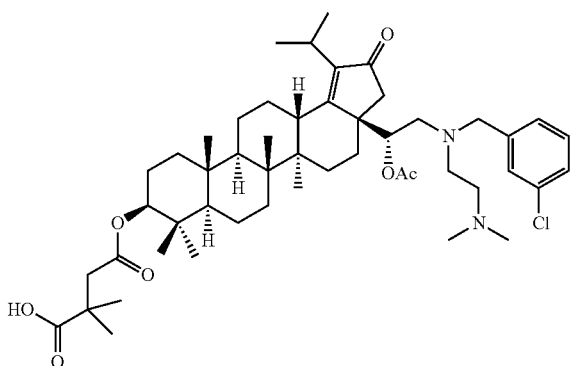
84

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Example 42 and 43

Compound 83 and 84

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-acetoxy-2-((3-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (83) and 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((3-chlorobenzyl)(ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (84)



To a solution of 2-(dimethylamino)acetaldehyde, hydrochloride (553 mg, 4.47 mmol) in methanol (10 ml) was added (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-(4-chlorobenzylamino)acetyl)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3a,4,5,5a,6,7,7a,8,9,10,11,11a,11b,12,13,13a-hexadecahydro-3H-cyclopenta[a]chrysen-2(5bH)-one (81) (15 g, 24.66 mmol). The reaction mixture was stirred at 40° C. for 2 h. The reaction was cooled to rt and sodium cyanoborohydride (7.75 g, 123 mmol) was added and the resultant mixture was stirred overnight. The reaction was diluted with ammonium chloride solution (40 ml), and extracted with DCM (60 ml×3). The combined organic layer was washed with brine (20 ml), dried over sodium sulfate,

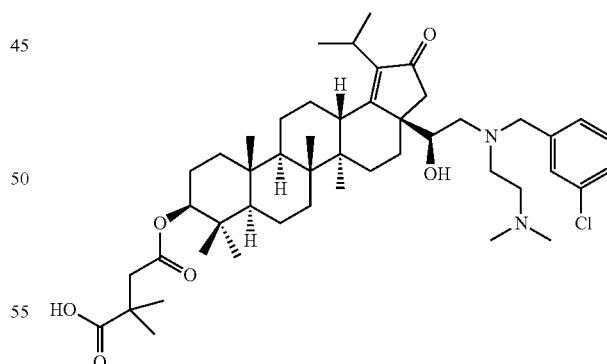
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filtered and concentrated in vacuo to afford crude product which was purified by preparative-HPLC to give 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-acetoxy-2-((3-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (83) (80 mg, 20%) and 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((3-chlorobenzyl)(ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (84) (14 mg, 3%) as their respective TFA salts. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. For 83; ¹H NMR (500 MHz, CHLOROFORM-d) δ=7.25-7.10 (m, 3H), 7.04 (d, J=3.8 Hz, 1H), 5.57 (d, J=9.1 Hz, 1H), 4.42 (dd, J=5.0, 10.7 Hz, 1H), 3.72 (d, J=13.9 Hz, 1H), 3.42 (d, J=14.2 Hz, 1H), 3.16-2.90 (m, 6H), 2.90-2.79 (m, 1H), 2.79-2.65 (m, 7H), 2.65-2.41 (m, 3H), 2.22 (d, J=18.3 Hz, 1H), 1.89 (s, 3H), 1.84-0.62 (m, 45H); LC/MS: m/z calculated 850.5, found 851.4 (M+1)⁺. For 84; ¹H NMR (400 MHz, METHANOL-d₄) δ=7.65 (s, 1H), 7.62-7.46 (m, 3H), 4.58-4.28 (m, 4H), 3.49-3.38 (m, 1H), 3.31-3.23 (m, 2H), 3.13-2.91 (m, 2H), 2.62 (q, J=15.9 Hz, 2H), 2.10-0.76 (m, 51H); LC/MS: m/z calculated 765.5, found 766.5 (M+1)⁺.

Example 44

Compound 85

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((3-Chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



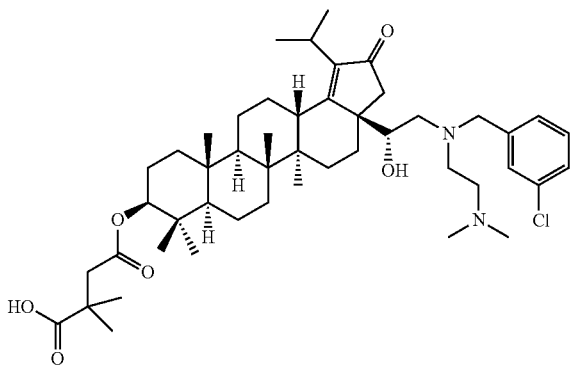
The title compound was made in a similar manner to Example 33. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, METHANOL-d₄) δ=7.57-7.31 (m, 4H), 4.50 (dd, J=5.0, 11.0 Hz, 1H), 4.28 (br. s., 1H), 4.02-3.69 (m, 2H), 3.53-3.36 (m, 1H), 3.32-3.07 (m, 4H), 3.08-2.85 (m, 2H), 2.78 (s, 6H), 2.73-2.51 (m, 3H), 2.45 (d, J=18.3 Hz, 1H), 2.13-0.75 (m, 46H); LC/MS: m/z calculated 808.5, found 809.5 (M+1)⁺.

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Example 45

Compound 86

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((3-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

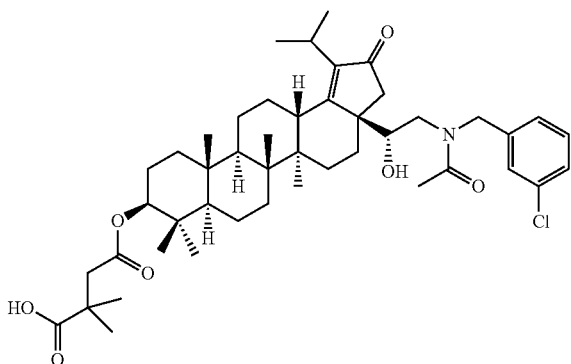


The title compound was made in a similar manner to example 33. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, METHANOL-*d*₄) δ=7.46-7.23 (m, 4H), 4.49 (dd, J=5.1, 10.9 Hz, 1H), 4.19 (d, J=10.0 Hz, 1H), 3.95-3.78 (m, 1H), 3.78-3.66 (m, 1H), 3.41-3.33 (m, 1H), 3.27-3.00 (m, 3H), 2.87 (s, 6H), 2.70-2.50 (m, 3H), 2.37 (br. s., 1H), 2.34-2.16 (m, 3H), 2.08-0.82 (m, 46H); LC/MS: m/z calculated 808.5, found 809.5 (M+1)⁺.

Example 46

Compound 87

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(N-(3-chlorobenzyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



The title compound was made in a similar manner to example 33 from compound 81. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. The compound exists as a mixture of rotomers. ¹H NMR (400 MHz, METHANOL-*d*₄) δ=7.42-7.04 (m, 4H),

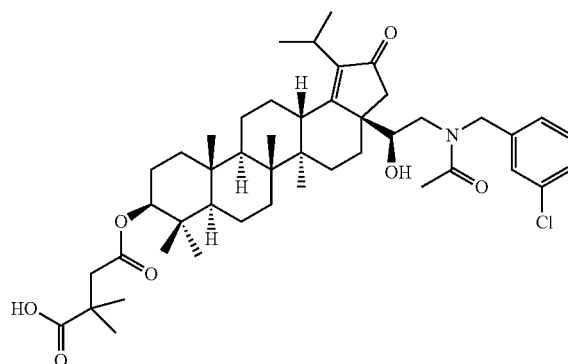
172

5.42-3.97 (m, 3H), 3.55-3.00 (m, 3H), 2.82-0.79 (m, 53H); LC/MS: m/z calculated 779.5, found 780.3 (M+1)⁺.

Example 47

Compound 88

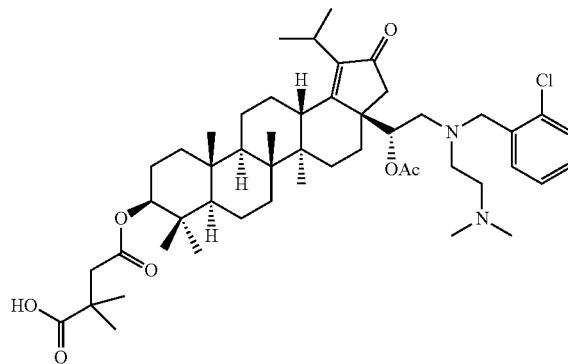
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(N-(3-chlorobenzyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



The title compound was made in a similar manner to example 33 from compound 80. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, METHANOL-*d*₄) δ=7.36-6.99 (m, 4H), 4.89-3.88 (m, 4H), 3.39-2.83 (m, 3H), 2.73-0.66 (m, 53H); LC/MS: m/z calculated 779.5, found 780.3 (M+1)⁺.

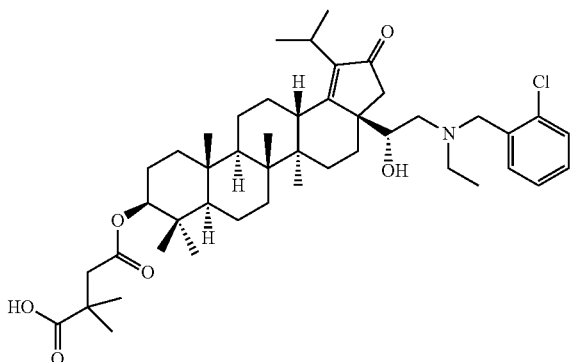
Example 48 and 49 Compounds 89 and 90

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-acetoxy-2-((2-chlorobenzyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (89) and 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-chlorobenzyl)(ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (90)



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-continued



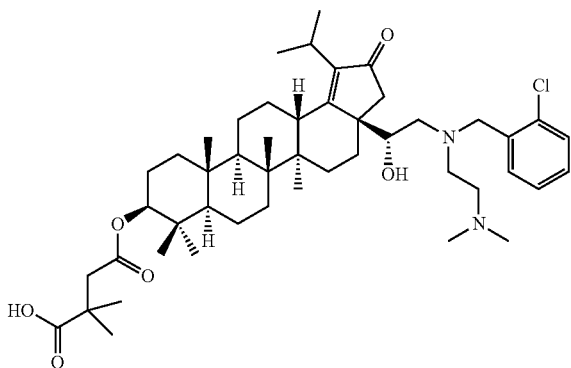
The title compounds were made in a similar manner to examples 42 and 43. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. For 89; ^1H NMR (400 MHz, CHLOROFORM- d_3) δ =7.42-7.18 (m, 4H), 5.70-5.56 (m, 1H), 4.57-4.42 (m, 1H), 3.83-3.51 (m, 2H), 3.21-2.85 (m, 3H), 2.79 (s, 6H), 2.74-2.54 (m, 3H), 2.54-2.23 (m, 4H), 2.15-0.65 (m, 50H);

LC/MS: m/z calculated 850.5. found 851.4 ($M+1$) $^+$. For 90; ^1H NMR (400 MHz, METHANOL- d_4) δ =7.77-7.43 (m, 4H), 4.69-4.27 (m, 4H), 3.62-3.37 (m, 2H), 3.26-3.10 (m, 1H), 2.97-2.82 (m, 1H), 2.61 (q, J =16.0 Hz, 2H), 2.27-2.10 (m, 1H), 2.10-0.77 (m, 51H); LC/MS: m/z calculated 765.5. found 766.3 ($M+1$) $^+$.

Example 50

Compound 91

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



The title compound was made in a similar manner to Example 33. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ^1H NMR (400 MHz, METHANOL- d_4) δ =7.55-7.42 (m, 2H), 7.42-7.32 (m, 2H), 4.49 (dd, J =5.5, 11.0 Hz, 1H), 4.43-4.30 (m, 1H), 4.00-3.89 (m, 1H), 3.87-3.76 (m, 1H), 3.42-3.34 (m, 1H), 3.24-2.91 (m, 3H), 2.91-2.51 (m, 10H), 2.52-2.17 (m,

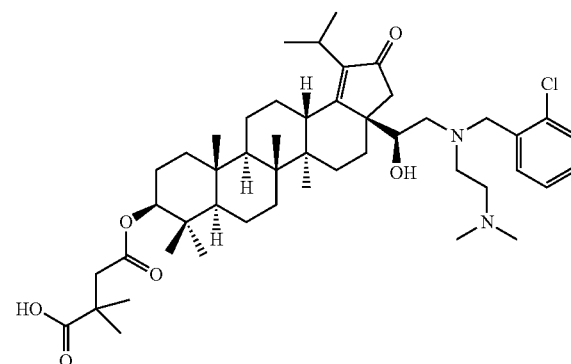
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4H), 2.11-1.84 (m, 2H), 1.84-0.78 (m, 44H); LC/MS: m/z calculated 808.5. found 809.4 ($M+1$) $^+$.

Example 51

Compound 92

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((2-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

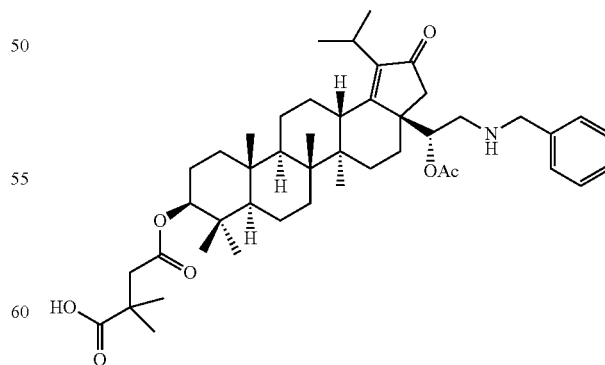


The title compound was made in a similar manner to Example 33. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ^1H NMR (400 MHz, METHANOL- d_4) δ =7.57-7.45 (m, 2H), 7.39 (dd, J =3.6, 5.6 Hz, 2H), 4.56-4.40 (m, 2H), 4.02 (d, J =12.8 Hz, 1H), 3.81 (d, J =12.8 Hz, 1H), 3.46-3.23 (m, 2H), 3.13-2.89 (m, 4H), 2.81-2.41 (m, 10H), 2.15-1.91 (m, 3H), 1.89-0.82 (m, 44H); LC/MS: m/z calculated 808.5. found 809.5 ($M+1$) $^+$.

Example 52

Compound 93

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-Acetoxy-2-(benzylamino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



The title compound was made as a TFA salt in a similar manner to Example 16. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ^1H NMR (500 MHz, DMSO- d_6) δ =12.17 (br. s., 1H), 9.49 (br. s., 1H), 9.19 (br. s., 1H), 7.66-7.28 (m, 5H), 5.86-5.53 (m,

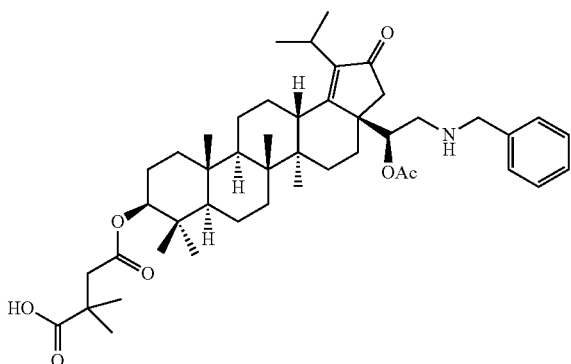
175

1H), 4.49-3.97 (m, 3H), 3.16-2.84 (m, 2H), 2.68-2.55 (m, 1H), 2.55-2.47 (m, 2H), 2.41 (d, J=19.5 Hz, 1H), 2.11 (s, 3H), 2.04-0.67 (m, 47H); LC/MS: m/z calculated 745.5. found 746.5 (M+1)⁺.

Example 53

Compound 94

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-Acetoxy-2-(benzylamino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

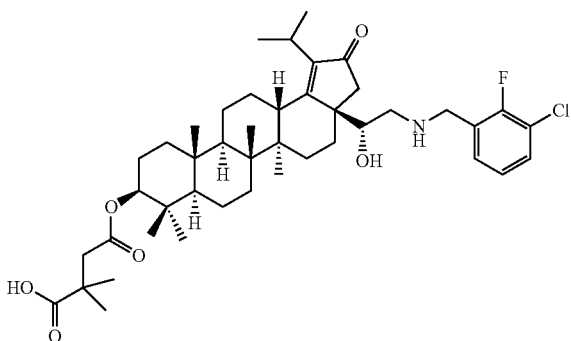


The title compound was made as a TFA salt in a similar manner to Example 16. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (500 MHz, CHLOROFORM-d) δ=7.41 (br. s., 5H), 5.81 (d, J=10.1 Hz, 1H), 4.48 (dd, J=5.5, 10.2 Hz, 1H), 4.25 (d, J=13.2 Hz, 1H), 4.06 (d, J=13.2 Hz, 1H), 3.27 (d, J=12.3 Hz, 1H), 3.14 (dt, J=6.8, 13.6 Hz, 1H), 3.08-2.85 (m, 2H), 2.74-2.62 (m, 1H), 2.62-2.54 (m, 1H), 2.36 (d, J=18.0 Hz, 1H), 1.99-0.63 (m, 49H); LC/MS: m/z calculated 745.5. found 746.5 (M+1)⁺.

Example 54

Compound 95

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((3-Chloro-2-fluorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



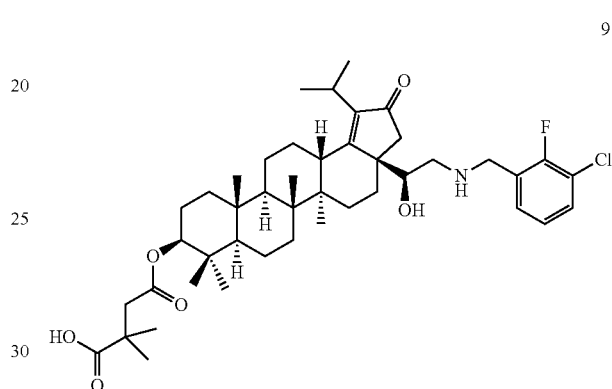
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The title compound was made as a TFA salt in a similar manner to Example 14. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 755.4. found 756.3 (M+1)⁺.

Example 55

Compound 96

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((3-chloro-2-fluorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

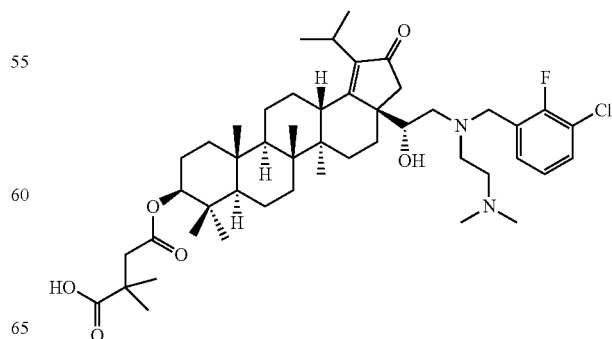


The title compound was made as a TFA salt in a similar manner to Example 14. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 755.4. found 756.2 (M+1)⁺.

Example 56

Compound 97

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((3-Chloro-2-fluorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



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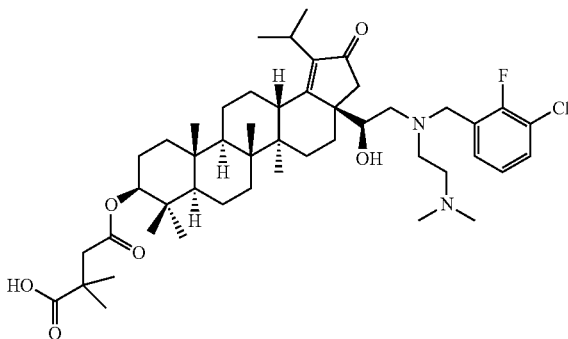
The title compound was made as a TFA salt in a similar manner to Example 18. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically.

¹H NMR (500 MHz, CHLOROFORM-d) δ=7.49-7.35 (m, 2H), 7.15 (t, J=7.7 Hz, 1H), 4.46 (dd, J=6.1, 9.9 Hz, 1H), 4.22 (d, J=10.4 Hz, 1H), 4.05 (d, J=13.9 Hz, 1H), 3.90 (d, J=13.6 Hz, 1H), 3.48 (br. s., 1H), 3.32-3.02 (m, 4H), 2.85 (br. s., 6H), 2.74-2.40 (m, 4H), 2.40-2.15 (m, 3H), 1.99-0.58 (m, 43H); LC/MS: m/z calculated 826.5. found 827.3 (M+1)⁺.

Example 57

Compound 98

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((3-Chloro-2-fluorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



The title compound was made as a TFA salt in a similar manner to Example 18. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically.

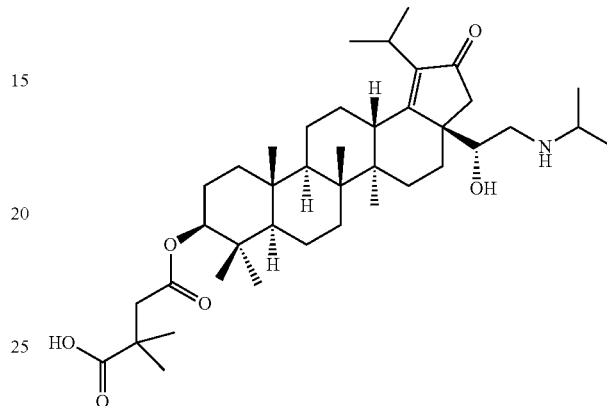
¹H NMR (500 MHz, CHLOROFORM-d) δ=7.56-7.32 (m, 2H), 7.16 (t, J=7.7 Hz, 1H), 4.53-4.38 (m, 1H), 4.28 (d, J=9.1 Hz, 1H), 4.13-3.87 (m, 2H), 3.44 (br. s., 1H), 3.33-2.91 (m, 5H), 2.93-2.21 (m, 11H), 2.09-1.95 (m, 1H), 1.95-0.65 (m, 45H); LC/MS: m/z calculated 826.5. found 827.3 (M+1)⁺.

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Example 58

Compound 99

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-Hydroxy-2-(isopropylamino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

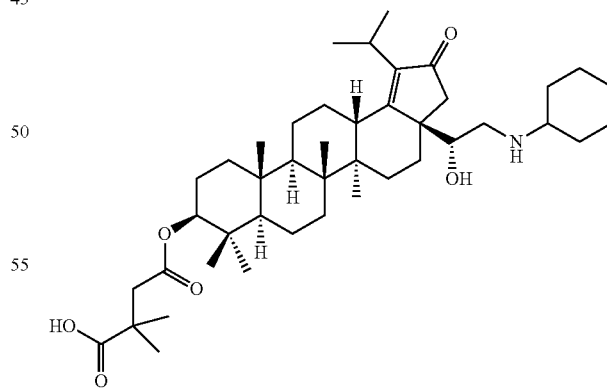


The title compound was made as a TFA salt in a similar manner to Example 18. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, CHLOROFORM-d) δ=10.30 (br. s., 1H), 4.71-4.26 (m, 2H), 3.49-2.98 (m, 2H), 2.87-2.42 (m, 6H), 2.42-2.21 (m, 1H), 2.07-0.68 (m, 53H); LC/MS: m/z calculated 655.5. found 656.5 (M+1)⁺.

Example 59

Compound 100

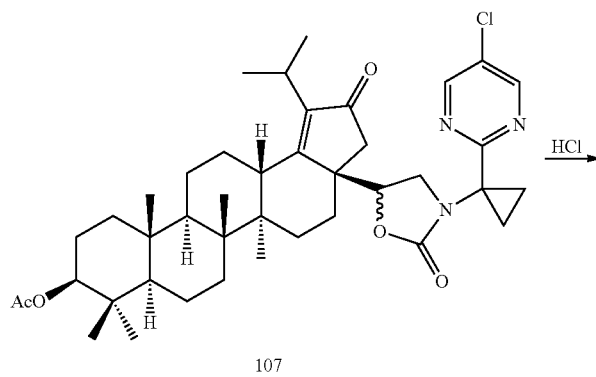
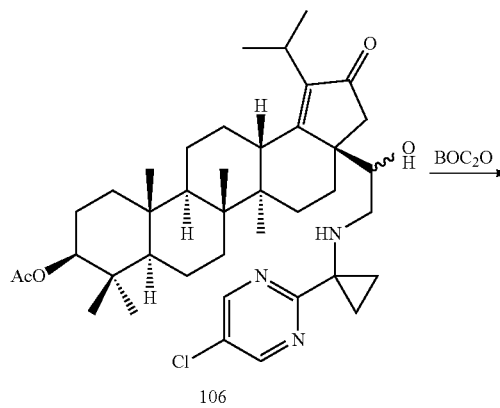
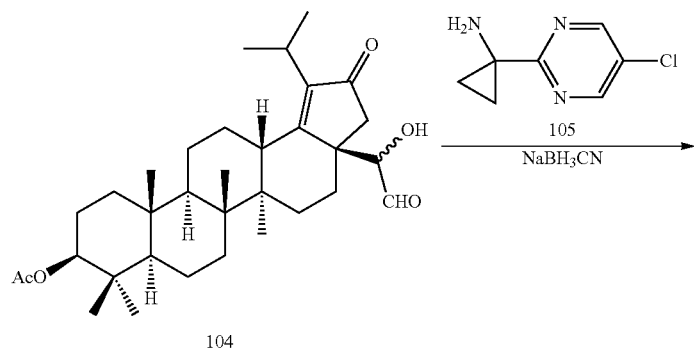
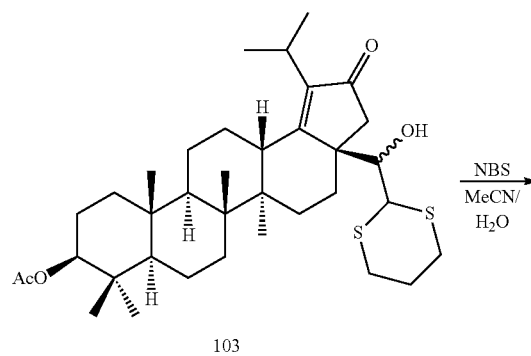
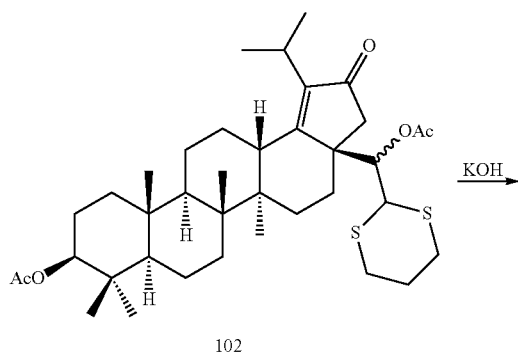
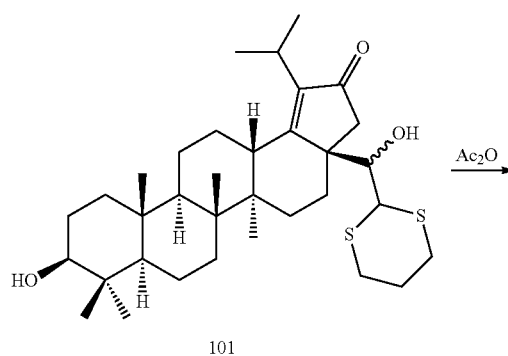
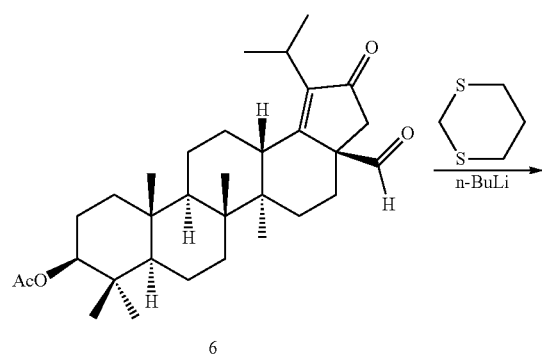
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(cyclohexylamino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



The title compound was made as a TFA salt in a similar manner to Example 18. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, CHLOROFORM-d) δ=10.25 (br. s., 1H), 7.12 (br. s., 1H), 4.67-4.34 (m, 2H), 3.29-3.03 (m, 1H), 2.92 (br. s., 1H), 2.83-2.42 (m, 6H), 2.42-2.26 (m, 1H), 2.11-0.72 (m, 55H); LC/MS: m/z calculated 695.5. found 696.4 (M+1)⁺.

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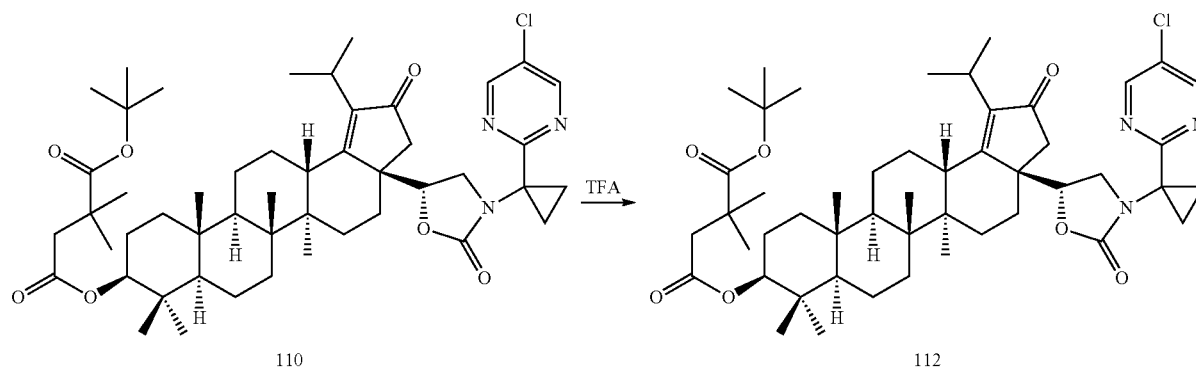
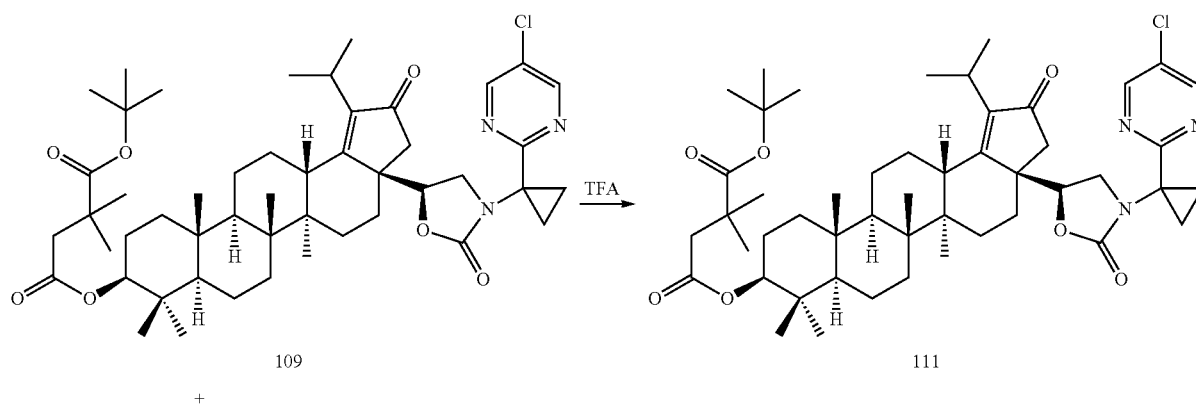
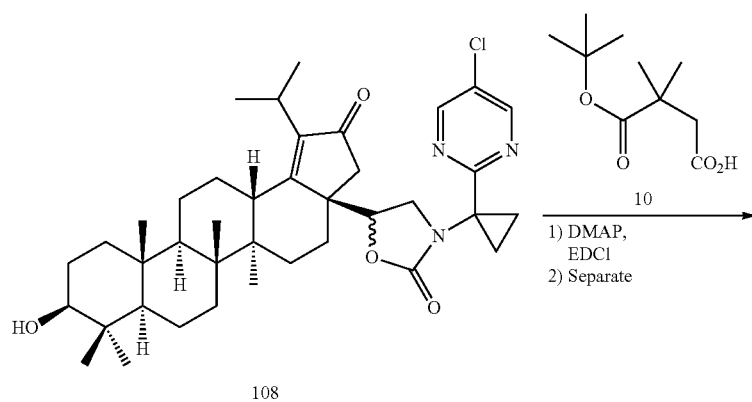
180



181

182

-continued

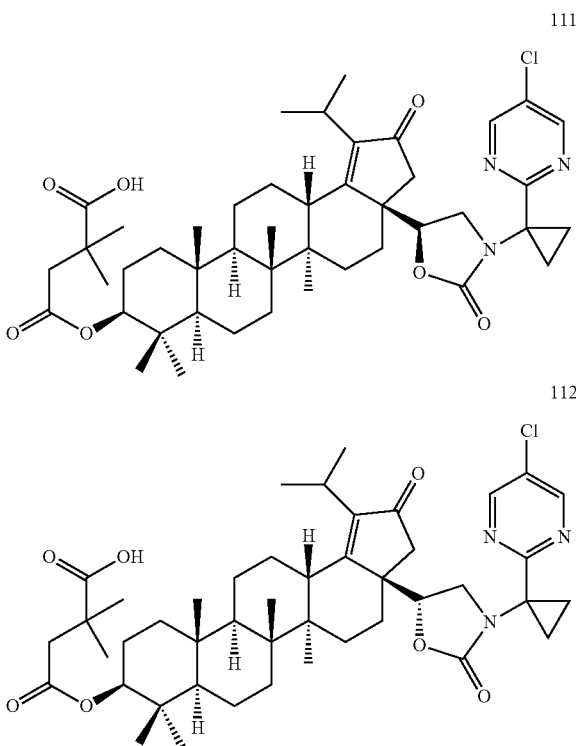


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Example 60 and 61

Compound III and 112

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (111) and 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (112)



Step A: Intermediate 101

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((1,3-Dithian-2-yl)(hydroxy)methyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-2-one

To a solution of 1,3-dithiane (5.7 g, 47.4 mmol) in anhydrous tetrahydrofuran (THF, 60 mL) under an atmosphere of nitrogen at -40°C . was slowly added a solution of *n*-BuLi (27 mL, 67.5 mmol). After the reaction mixture was stirred at -20°C . for another 2 h, a solution of the intermediate 6 (4.2 g, 8.46 mmol) in anhydrous THF (40 mL) was slowly added under an atmosphere of nitrogen at -70°C . The reaction was then stirred at -78°C . for 1 h before it was quenched with a saturated solution of NaHCO_3 . Extraction was conducted

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with EtOAc and the organic phase was washed with water (50 mL), saturated brine (50 mL), dried over sodium sulfate, and evaporated under reduced pressure to provide a crude product, which was purified by column chromatography on silica gel (PE:EtOAc=8:1 to 4:1) to afford the intermediate 101 (3.0 g, 5.22 mmol, 61.7%). LC/MS: *m/z* calculated 574.4. found 575.0 ($\text{M}+1$)⁺.

Step B: Intermediate 102

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(Acetoxy(1,3-dithian-2-yl)methyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of the intermediate 101 (3.5 g, 6.09 mmol), Et_3N (2.55 mL, 18.26 mmol), and DMAP (0.149 g, 1.218 mmol) in DCM (40 mL) was added Ac_2O (3.45 mL, 36.5 mmol) at room temperature. After stirring at 50°C . for 2 h, the reaction mixture was quenched with water. The organic phase was washed with water (100 mL), dried over sodium sulfate, and evaporated under reduced pressure to provide the intermediate 102 (3.41 g, 85%). LC/MS: *m/z* calculated 658.4. found 659.1 ($\text{M}+1$)⁺.

Step C: Intermediate 103

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((1,3-Dithian-2-yl)(hydroxy)methyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

A solution of 102 (6.7 g, 10.17 mmol) and potassium hydroxide (1.141 g, 20.33 mmol) in a mixture 1:1 of toluene and ethanol (100 mL) was stirred vigorously at rt for 1 hr. The reaction mixture was neutralized with aqueous 1N HCl to pH 7 and reduced to dryness. The residue was purified on a silica gel using Petroleum ether/EtOAc (5:1) to yield (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((1,3-dithian-2-yl)(hydroxy)methyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (103) (3.4 g, 5.01 mmol, 49%) as a light yellow compound. LC/MS: *m/z* calculated 616.4. found 617.3 ($\text{M}+1$)⁺.

Step D: Intermediate 104

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(1-hydroxy-2-oxoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of 103 (1.2 g, 1.945 mmol) in acetonitrile (20 mL) and water (5.00 mL) stirred in air at rt was added NBS (1.385 g, 7.78 mmol) in one charge. The reaction mixture was stirred at rt for 0.5 h, then quenched with Na_2SO_3 (solid), concentrated and the residue was extracted with EtOAc. The organic phase was washed with water and saturated brine, dried over sodium sulphate and concentrated in vacuo to give (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(1-hydroxy-2-oxoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (104) (1.09 g, 1.083 mmol, 55.7% yield) as a light yellow solid which was used without further purification.

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Step E: Intermediate 106

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((1-(5-Chloropyrimidin-2-yl)cyclopropyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(1-hydroxy-2-oxoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (104) (545 mg, 1.035 mmol) and 1-(5-chloropyrimidin-2-yl)cyclopropanamine, hydrochloride (105) (213 mg, 1.035 mmol) in methanol (5 ml) and 1,2-dichloroethane (5 ml) was added zinc chloride (141 mg, 1.035 mmol). The reaction mixture was stirred at room temperature overnight, and then sodium cyanoborohydride (65.0 mg, 1.035 mmol) was added. The reaction mixture was allowed to stir for 1 h, then silica gel was added to the mixture and the solvents removed in vacuo to give the residue-silica gel powder which was purified on a silica gel column using petroleum ether/EtOAc (5:1 to 3:1) to afford (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((1-(5-chloropyrimidin-2-yl)cyclopropyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (105) as a mixture of diastereomers (200 mg, 0.166 mmol, 16.04% yield) as a yellow foam. LC/MS: m/z calculated 679.4. found 680.3 (M+1)⁺.

Step F: Intermediate 107

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(3-(1-(5-Chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((1-(5-chloropyrimidin-2-yl)cyclopropyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (106) (400 mg, 0.588 mmol) in dichloromethane (15 ml) stirred at rt was added BOC₂O (1.365 ml, 5.88 mmol). The reaction mixture was stirred at rt overnight then evaporated under reduced pressure and the residue was subjected to a silica gel chromatography with petroleum ether/EtOAc (6:1 to 3:1) to give (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (107) (350 mg, 0.496 mmol, 84% yield) as a white solid.

Step G: Intermediate 108

3-(1-(5-Chloropyrimidin-2-yl)cyclopropyl)-5-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)oxazolidin-2-one

To a solution of (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (107)

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(350 mg, 0.496 mmol) in 1,4-dioxane (10 mL) and methanol (5 mL) was added hydrochloric acid (5 mL, 165 mmol). The reaction mixture was stirred at 40° C. overnight. The solvents were removed under reduced pressure and taken up in DCM (100 ml), washed with sat. NaHCO₃ (20 ml), water (20 ml) and brine (20 ml), dried over sodium sulfate, filtered and concentrated to give residue, which was subjected to a silica gel column eluting with petroleum ether/EtOAc (6:1 to 3:1) to give 3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-5-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)oxazolidin-2-one (130 mg, 0.087 mmol, 17%) as a white solid. LC/MS: m/z calculated 663.4. found 664.3 (M+1)⁺.

Step H: Intermediates 109 and 110

1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (109) and 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (110)

A mixture of 4-tert-butoxy-3,3-dimethyl-4-oxobutanoic acid 10 (119 mg, 0.587 mmol), 3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-5-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)oxazolidin-2-one (108) (130 mg, 0.196 mmol), EDC (188 mg, 0.978 mmol) and DMAP (71.7 mg, 0.587 mmol) in DCM (5 mL) was stirred at rt overnight. After the reaction finished, the mixture was diluted with DCM (25 ml), washed with water (2×15 ml) and brine (20 ml), dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/EtOAc (6:1 to 3:1) as eluent to give the two diastereomeric products 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (109) and 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (110) in the amounts of (80 mg, 45%) and (50 mg, 22%) as white solids. The stereochemical assignments for each diastereomer were not made. Compound A (tentatively designated as 109): LC/MS: m/z calculated 847.5. found 848.3 (M+1)⁺. Compound B (tentatively designated as 110): LC/MS: m/z calculated 847.5. found 848 (M+1)⁺.

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Step I: Compound 111

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

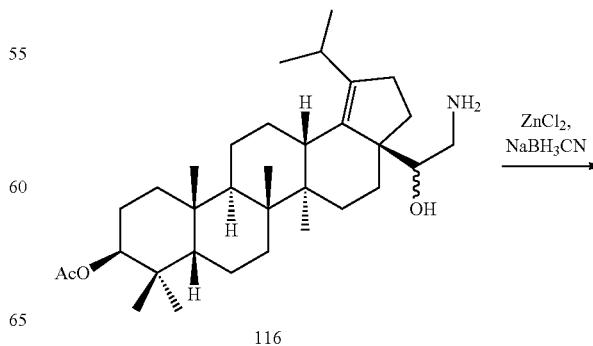
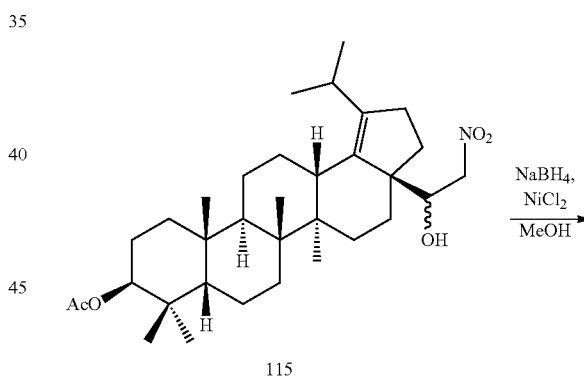
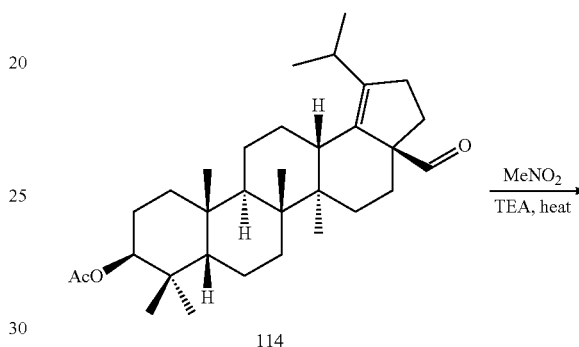
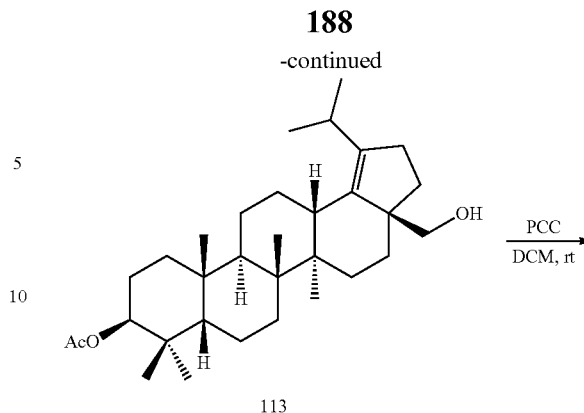
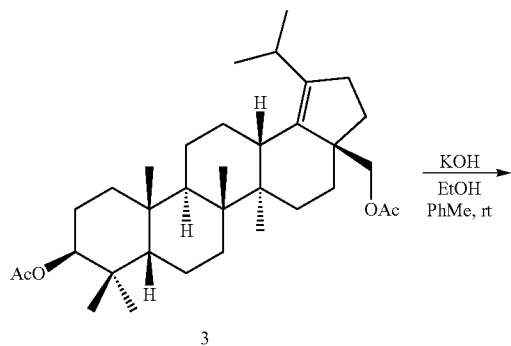
To a solution of 1-tert-butyl 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (109) (80 mg, 0.094 mmol) in DCM (10 mL) was added TFA (1 mL, 0.094 mmol). The reaction mixture was stirred at rt overnight, then diluted with DCM (20 mL) and washed with water (2x15 mL), saturated sodium bicarbonate solution (20 mL) and brine (20 mL), dried over sodium sulfate, filtered and concentrated to get a residue. The residue was purified on silica gel using petroleum ether/EtOAc (4:1 to 1:1) as eluent to give the product 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (111) (50 mg, 67%) as a white solid. This material was lyophilized to give a white powder. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, CHLOROFORM-d) δ=8.58 (s, 2H), 5.04 (t, J=8.5 Hz, 1H), 4.51 (dd, J=4.6, 10.9 Hz, 1H), 3.41-3.04 (m, 4H), 2.75-2.44 (m, 3H), 2.36 (d, J=13.3 Hz, 1H), 2.12-0.72 (m, 49H); LC/MS: m/z calculated 791.4, found 792.3 (M+1)⁺.

Step J: Compound 112

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-3-(1-(5-chloropyrimidin-2-yl)cyclopropyl)-2-oxooxazolidin-5-yl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

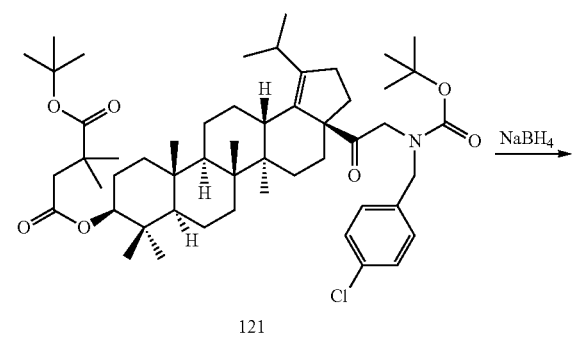
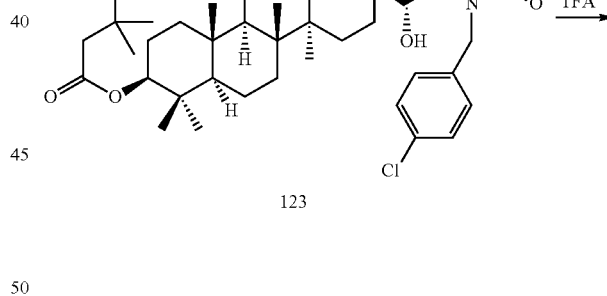
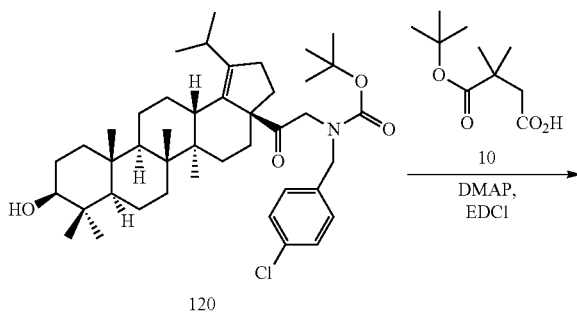
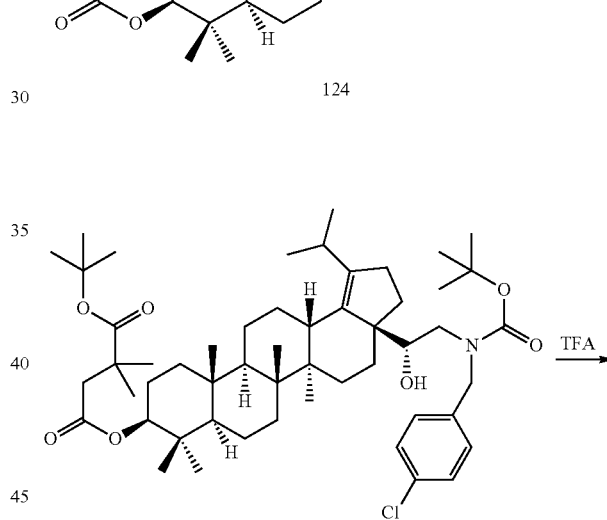
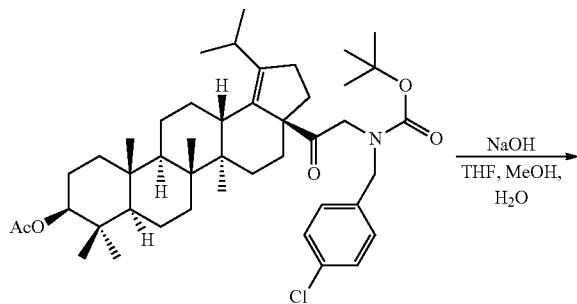
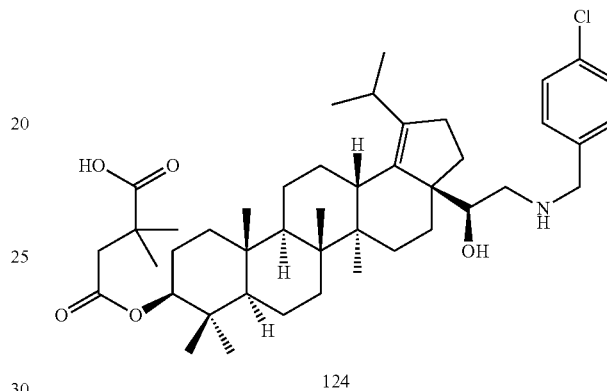
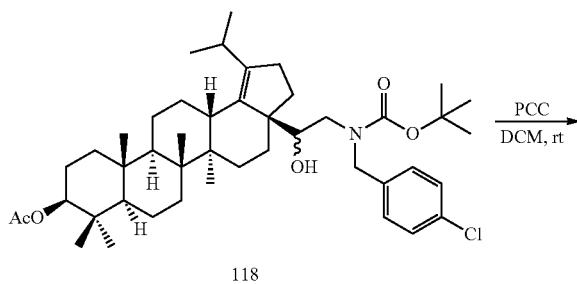
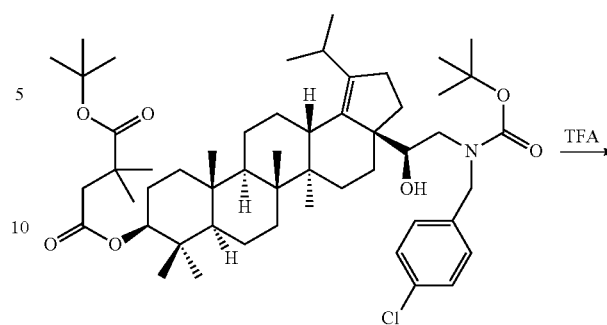
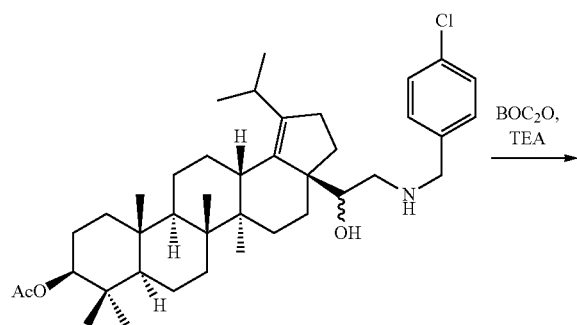
The title compound was made in a similar manner to that described for compound III. Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. ¹H NMR (400 MHz, CHLOROFORM-d) δ=8.59 (s, 2H), 5.10 (t, J=8.8 Hz, 1H), 4.52 (dd, J=5.3, 10.8 Hz, 1H), 3.70-3.54 (m, 2H), 3.28-3.10 (m, 2H), 3.08-2.92 (m, 2H), 2.77-2.53 (m, 2H), 2.14-0.58 (m, 49H);

LC/MS: m/z calculated 791.4, found 792.3 (M+1)⁺.



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-continued

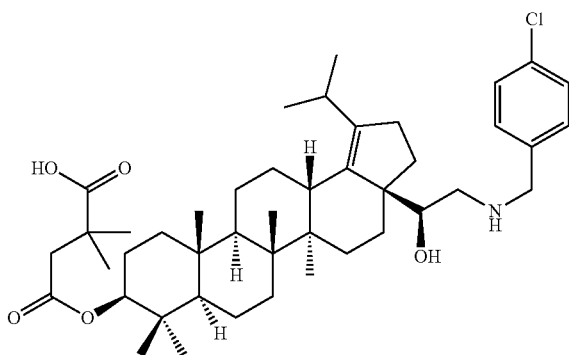


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Example 62

Compound 124

4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-Chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



Step A: Intermediate 113

(3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(Hydroxymethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of the intermediate 3 (5 g, 7.59 mmol) in EtOH (100 mL) and toluene (100 mL) was added KOH (0.51 g, 9.11 mmol). After stirring at room temperature for 4 h, the reaction mixture was then partitioned between water (500 mL) and EtOAc (500 mL). The organic phase was washed with water (200 mL×3), brine (100 mL), and dried over sodium sulfate. Removal of the solvent provided a residue, which was purified by column chromatography on silica gel (Hex:EtOAc=6:1 to 4:1) to afford the intermediate 113 (2.5 g, 67.9%) as a white solid. ¹H NMR (400 Hz, CDCl₃) δ ppm 4.50-4.67 (1H, m), 3.68 (1H, d, J=10.4 Hz), 3.32 (1H, d, J=10.4 Hz), 3.23-3.15 (1H, m), 2.42-2.28 (3H, m), 2.05 (3H, s), 2.02-1.89 (2H, m), 1.77-0.83 (40H, m).

Step B: Intermediate 114

(3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-Formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of the intermediate 113 (3 g, 6.19 mmol) in DCM (75 mL) at room temperature were added PCC (4 g, 18.57 mmol) and silica gel (3.0 g). After stirring at room temperature for 2 h, the reaction was quenched with water (100 mL). The organic phase was separated, washed with saturated sodium bicarbonate (50 mL), dried over sodium sulfate and concentrated in vacuo to provide a residue, which was purified by column chromatography on silica gel (Hex: EtOAc=10:1) to afford the intermediate 114 (3 g, 100%) as a white solid. ¹H NMR (400 Hz, CDCl₃) δ ppm 9.43 (1H, s),

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4.50-4.46 (1H, m), 3.25-3.21 (1H, m), 2.43-2.02 (5H, m), 2.04 (3H, m), 2.00-1.93 (1H, m), 1.75-0.81 (38H, m).

Step C: Intermediate 115

(3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(1-Hydroxy-2-nitroethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of the intermediate 114 (5 g, 10.36 mmol) in MeNO₂ (128 mL, 2382 mmol) was added Et₃N (10.11 mL, 72.5 mmol). After it was stirred at 60° C. overnight, the reaction mixture was partitioned between water and EtOAc (100 mL each). The organic phase was washed with water (20 mL×3), brine (20 mL), and dried over sodium sulfate. Removal of the solvent provided a residue, which was purified by column chromatography on silica gel (Hex: EtOAc=10:1 to 6:1) to afford the intermediate 115 (2.8 g, 49.7%) as a white powder. LC/MS: m/z calculated 543.4, found 566.3 (M+Na⁺)⁺.

Step D: Intermediate 116

(3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-Amino-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of the intermediate 115 (2.8 g, 5.15 mmol) in MeOH (166 mL) were added nickel(II) chloride (1.67 g, 12.87 mmol) and sodium borohydride (4.87 g, 129 mmol) at 0° C. for 10 min, the reaction mixture was partitioned between water and EtOAc (200 mL each), and the organic phase was washed with water (100 mL×3), brine (50 mL), and dried over sodium sulfate. Removal of the solvent provided the intermediate 116 (2.65 g, 100%) as a solid.

LC/MS: m/z calculated 513.4, found 514.3 (M+1)⁺.

Step E: Intermediate 118

(3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-Butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of the intermediate 116 (350 mg, 0.613 mmol) and 4-chlorobenzaldehyde (86 mg, 0.613 mmol) in MeOH (15 mL) and dichloroethane (DCE, 15 mL) was added zinc chloride (50.1 mg, 0.368 mmol). After the reaction mixture was stirred at 80° C. for 1 h and cooled down to room temperature, sodium cyanoborohydride (57.8 mg, 0.92 mmol) was added. The resulting mixture was stirred at room temperature for another 1 h to provide the intermediate 117.

To the reaction mixture obtained above were added Et₃N (0.18 mL, 1.38 mmol) and di-tert-butyl dicarbonate (0.157 mL, 0.674 mmol). After stirring at room temperature for 30 min, the reaction mixture was partitioned between water (20 mL) and EtOAc (100 mL). The organic phase was washed with water (30 mL×3), brine (20 mL), and dried over sodium sulfate. Removal of the solvent provided a residue, which was purified by column chromatography on silica gel (Hex: EtOAc=15:1) to afford the intermediate 118 (125 mg, 27.6%) as a white solid.

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Step F: Intermediate 119

(3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a solution of the intermediate 118 (120 mg, 0.162 mmol) in DCM (10 mL) were added PCC (35 mg, 0.162 mmol) and silica gel (100 mg). After stirring at room temperature for 2 h, the insoluble material was removed by filtration and the filtrate was concentrated to afford the intermediate 119 (110 mg, 92%) as a white solid.

Step G: Intermediate 120

tert-butyl 4-Chlorobenzyl(2-((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-oxoethyl)carbamate

To a solution of NaOH (597 mg, 14.94 mmol) in MeOH (1 mL), THF (1 mL), and water (0.5 mL) was added the intermediate 119 (110 mg, 0.149 mmol). After stirring at room temperature for 1 h, the reaction was diluted with water (20 mL), and extracted with EtOAc (50 mL). The organic phase was washed with brine (20 mL), dried over sodium sulfate, and evaporated in vacuo to afford the intermediate 120 (100 mg, 96%) as a white solid.

Step H: Intermediate 121

4-((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate

To a solution of 4-tert-butoxy-3,3-dimethyl-4-oxobutanoic acid 10 (1.648 g, 8.15 mmol), DMAP (0.995 g, 8.15 mmol) in DCM (15 mL) stirred at rt was added EDCl (2.60 g, 13.58 mmol). The reaction mixture was stirred at rt. for 2 h. Then tert-butyl 4-chlorobenzyl(2-((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-yl)-2-oxoethyl) carbamate 120 (1.886 g, 2.72 mmol) was added to the reaction. The reaction mixture was stirred at rt overnight. Upon completion, the mixture was washed with water (25 mL×2) and brine, dried over sodium sulfate filtered through a short silica gel column and evaporated in vacuo to give the crude product which was further purified on a silica gel column using petroleum ether/EtOAc (50:1 to 10:1) to give intermediate 121 (2.37 g, 99%) as white foam.

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Step I: Intermediates 122 and 123

4-((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate (122) and 4-((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate (123)

To a solution of and 4-((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)acetyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate (121) (791 mg, 0.90 mmol) in MeOH (10 mL) and THF (10.00 mL) stirred at 0° C. was added NaBH₄ (170 mg, 4.50 mmol). The reaction mixture was stirred at rt for 2 h until starting material had disappeared. Upon completion, silica gel was added and the mixture evaporated to dryness and purified by silica gel chromatography (petroleum ether/EtOAc, 40:1 to 10:1) to give the two diastereomeric products: 4-((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate and 4-((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((tert-butoxycarbonyl)(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)-1-tert-butyl 2,2-dimethylsuccinate. Stereochemistry was not confirmed but the diastereomers were produced in the amount of (410 mg, 52%, tentatively assigned as compound 122) and (77 mg, 10%, tentatively assigned as compound 123) as white foams.

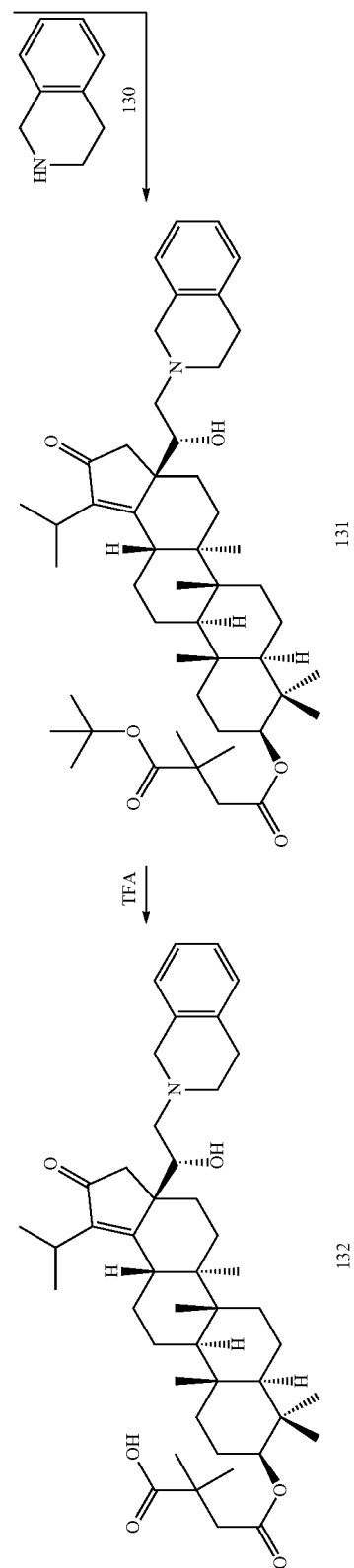
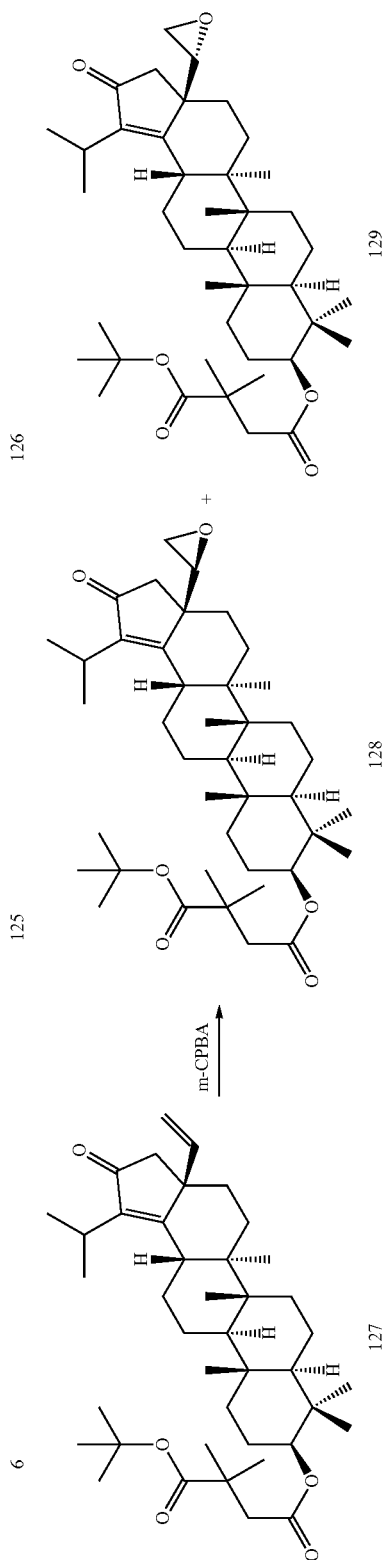
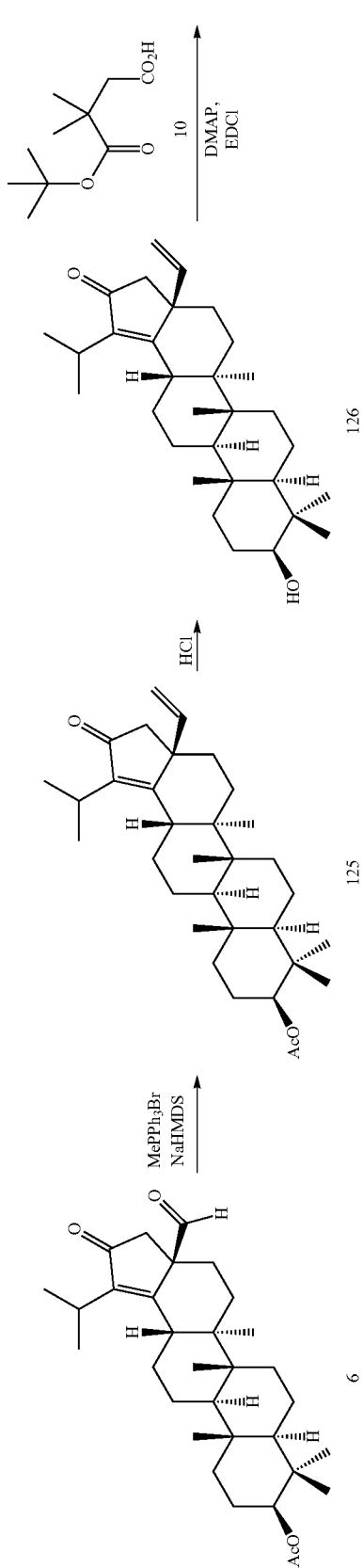
Step J: Compound 124

4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

To a solution of 122 (410 mg, 0.466 mmol) in DCM (10 mL) was added TFA (2 mL, 26.0 mmol). The reaction mixture was stirred at rt for 2 h. The reaction mixture was concentrated to dryness and purified by preparative-HPLC to afford 4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid, trifluoroacetic acid salt (124) (185 mg, 0.221 mmol, 47.4% yield) as white solid. ¹H NMR (500 MHz, CHLOROFORM-d) δ=7.36 (q, J=8.5 Hz, 4H), 4.58-4.41 (m, 1H), 4.41-4.31 (m, 1H), 4.20-3.97 (m, 2H), 3.23-3.05 (m, 2H), 2.85-2.66 (m, 2H), 2.56 (d, J=16.1 Hz, 1H), 2.51-2.38 (m, 1H), 2.34-2.19 (m, 2H), 1.93-1.82 (m, 1H), 1.83-0.67 (m, 46H); LC/MS: m/z calculated 723.5, found 724.3 (M+1)⁺.

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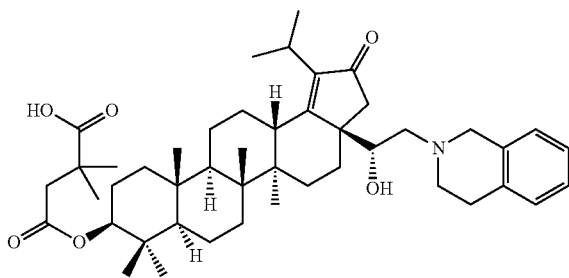


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Example 63

Compound 132

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
(R)-2-(3,4-dihydroisoquinolin-2(1H)-yl)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid



Step A: Intermediate 125

(3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-vinyl-3,3a,
4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octa-
decahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a cold (-78°C .) solution of methyltriphenylphospho-
nium bromide (8.63 g, 24.16 mmol) in THF (30 mL) was
added lithium bis(trimethylsilyl)amide (4.4 g, 24.1 mmol) in
THF dropwise. The reaction was stirred at -78°C . for 1 h,
then 6 (10.0 g, 20.1 mmol) in THF (60 mL) was added. The
mixture was allowed to warm to rt and stirred for 1 h. TLC
indicated the reaction was complete. 2N HCl was added to the
mixture and it was extracted with ethyl acetate and washed with
water and brine. The organic phase was dried with Na_2SO_4
followed by filtration and concentration followed by precipi-
tation of the desired product (10 g of 85% purity, 85% chemi-
cal yield) with 5% EtOAc/petroleum ether.

Step B: Intermediate 126

(3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-3a-vinyl-3,
3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-2-one

To a solution of 125 (16 g, 32.3 mmol) in 1,4-dioxane (300
mL) and MeOH (30 mL) stirred at rt was added HCl (37%)
(150 mL, 32.3 mmol). The reaction mixture was stirred at 60°C .
for 3 h. TLC and LCMS indicated the starting material was
consumed completely. Water was added and the volatiles
were concentrated, a resultant precipitate was filtered and
washed with water. The cake was dried to give 126 (14 g,
81%).

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Step C: Intermediate 127

1-tert-butyl 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,
13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3a-vinyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,
13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-
yl) 2,2-dimethylsuccinate

To a solution of 10 (14.52 g, 71.8 mmol), DMAP (10.52 g,
86 mmol) and 126 (13 g, 28.7 mmol) in dichloromethane (150
mL) was added EDC (27.5 g, 144 mmol). The mixture was
stirred at rt for 2 h, at which time TLC indicated the reaction
was complete. The reaction was washed with 2N HCl, and
brine. The organics were dried with Na_2SO_4 , filtered and
concentrated. The residue was purified by silica gel chroma-
tography to give 127 (9.5 g, 49%) along with an additional 4
g impure product requiring repurification prior to further use.

Step D: Intermediates 128 and 129

1-tert-butyl 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,
13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3a-
(S)-oxiran-2-yl)-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl) 2,2-dimethylsuccinate (128) and
1-tert-butyl 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,
13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3a-
(R)-oxiran-2-yl)-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl) 2,2-dimethylsuccinate (129)

To a solution of 127 (8.5 g, 13.34 mmol) in DCM (90 mL)
at rt was added m-CPBA (5.42 g, 26.7 mmol). The reaction
mixture was stirred at rt overnight. The mixture was further
diluted with DCM 150 mL then washed with saturated
 NaHCO_3 , water and brine (note for safety reasons this the
excess peroxide should be neutralized but was not in this
specific procedure). The organic phase was concentrated and
purified by silica gel chromatography (EtOAc/PE 5% to 15%)
to give 128 (2.0 g, 21%) and 129 (800 mg, 8%) along with 2.4
g of recovered starting material. For 128: ^1H NMR (500 MHz,
CHLOROFORM- d) δ =4.51 (dd, J =5.4, 11.3 Hz, 1H), 3.26-
3.12 (m, 3H), 2.66 (t, J =4.4 Hz, 1H), 2.54 (s, 2H), 2.35 (dd,
 J =2.7, 4.6 Hz, 1H), 2.18 (d, J =18.3 Hz, 1H), 2.12-1.93 (m,
3H), 1.91-0.74 (m, 52H); LC/MS: m/z calculated 652.5.
found 653.3 ($M+1$) $^+$. For 129: ^1H NMR (500 MHz, CHLO-
ROFORM- d) δ =4.51 (dd, J =5.0, 11.3 Hz, 1H), 3.26-3.07 (m,
2H), 3.00 (dd, J =3.2, 12.6 Hz, 1H), 2.69 (t, J =4.3 Hz, 1H),
2.59-2.41 (m, 3H), 2.21-0.76 (m, 56H); LC/MS: m/z calcu-
lated 652.5. found 653.3 ($M+1$) $^+$.

Step E: Intermediate 131

1-tert-butyl 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,
13aS)-3a-((R)-2-(3,4-dihydroisoquinolin-2(1H)-yl)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl) 2,2-dimethylsuccinate

To a solution of 1-tert-butyl 4-(((3aR,5aR,5bR,7aR,9S,
11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
3a-((R)-oxiran-2-yl)-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl) 2,2-dimethylsuccinate (0.2 g, 0.306 mmol) in

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tert-butanol (3 mL) was added 1,2,3,4-tetrahydroisoquinoline (0.408 g, 3.06 mmol). The reaction mixture was stirred at 100° C. for 5 h. Upon completion and cooling, EtOAc was added and the mixture was washed with 4N HCl, and brine, then dried with Na₂SO₄, filtered and concentrated to give 132 (200 mg, 66%) which was used without further purification. LC/MS: m/z calculated 785.6, found 786.5 (M+1)⁺.

Step F: Compound 132

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(3,4-dihydroisoquinolin-2(1H)-yl)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

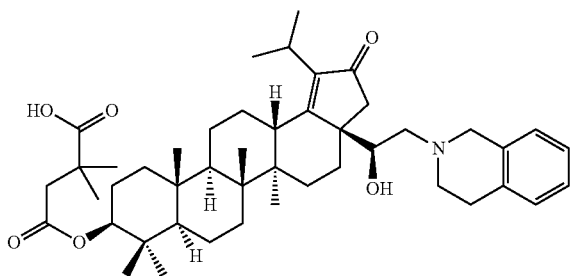
To a solution of 131 (0.2 g, 0.254 mmol) in DCM (2 mL) was added TFA (1 mL, 12.98 mmol). The reaction mixture was stirred at rt for 1 h then concentrated. The residue was purified by preparative-HPLC to give the title compound (106 mg, 48%) as a TFA salt as white solid. ¹H NMR (500 MHz, METHANOL-d₄) δ=7.43-7.15 (m, 4H), 4.66-4.41 (m, 4H), 3.28-3.05 (m, 3H), 3.05-2.83 (m, 2H), 2.73-2.52 (m, 3H), 2.30 (d, J=13.9 Hz, 1H), 2.16-2.03 (m, 1H), 2.00-0.72 (m, 48H); LC/MS: m/z calculated 729.5, found 730.5 (M+1)⁺.

The Examples below were made in a similar manner to the above examples or via combinations or re-ordering of the methods described and/or usage of other methods well known to those skilled in the art.

Example 64

Compound 133

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(3,4-dihydroisoquinolin-2(1H)-yl)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



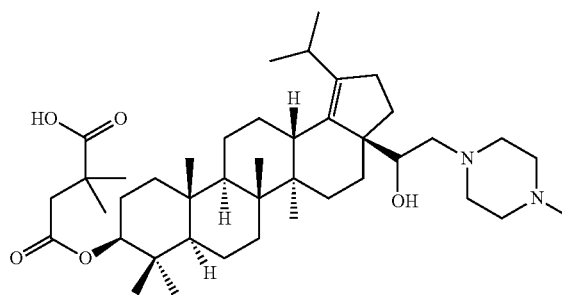
200

Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 729.5, found 730.5 (M+1)⁺.

Example 65

Compound 134

4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-hydroxy-2-(4-methylpiperazin-1-yl)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

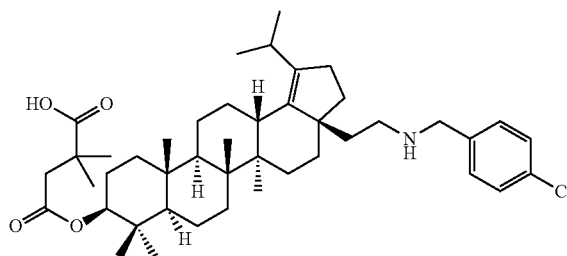


Isolated as a mixture of diastereomers. LC/MS: m/z calculated 682.53, found 683.5 (M+1)⁺.

Example 66

Compound 135

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((2-((4-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



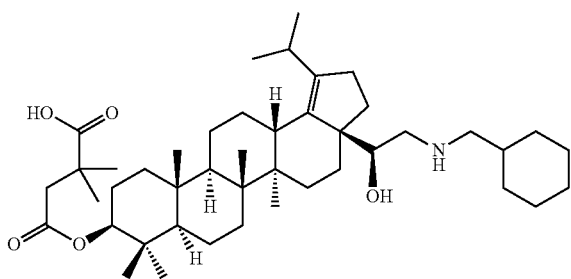
LC/MS: m/z calculated 707.5, found 708.3 (M+1)⁺.

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Example 67

Compound 136

4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((cyclohexylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

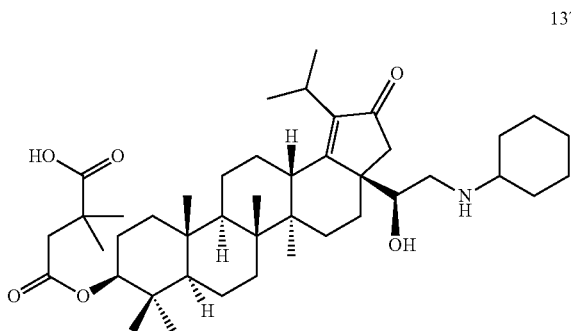


Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 695.6. found 696.5 (M+1)⁺.

Example 68

Compound 137

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(cyclohexylamino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



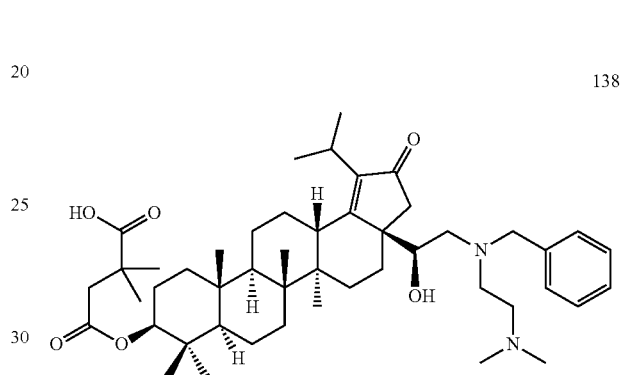
202

Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 695.5. found 696.5 (M+1)⁺.

Example 69

Compound 138

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(benzyl(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

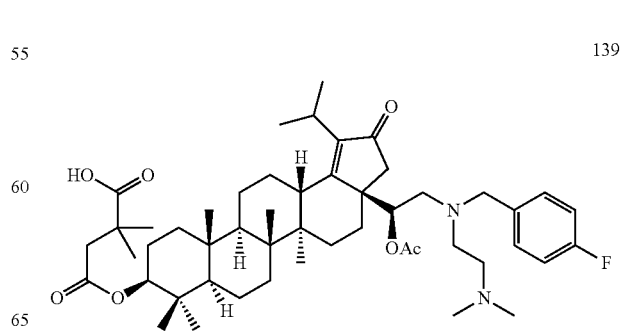


Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 774.6. found 775.5 (M+1)⁺.

Example 70

Compound 139

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-acetoxy-2-((2-(dimethylamino)ethyl)(4-fluorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



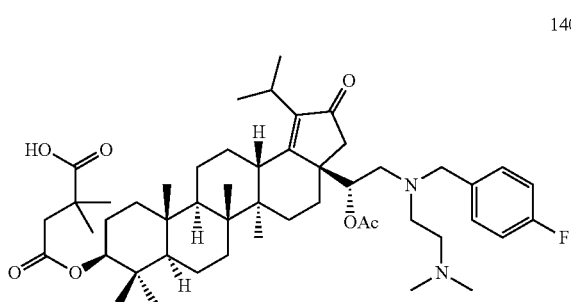
203

Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 834.6. found 835 (M+1)⁺.

Example 71

Compound 140

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-acetoxy-2-((2-(dimethylamino)ethyl)(4-fluorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

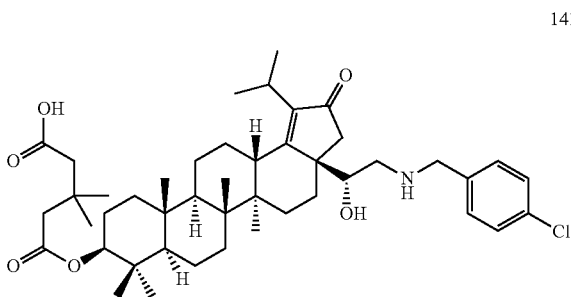


Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 834.6. found 835 (M+1)⁺.

Example 72

Compound 141

5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid



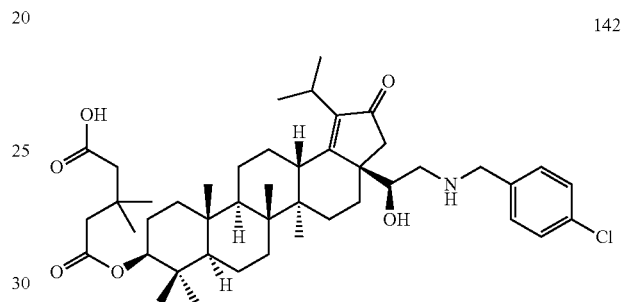
204

Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 751.5. found 752.3 (M+1)⁺.

Example 73

Compound 142

5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid

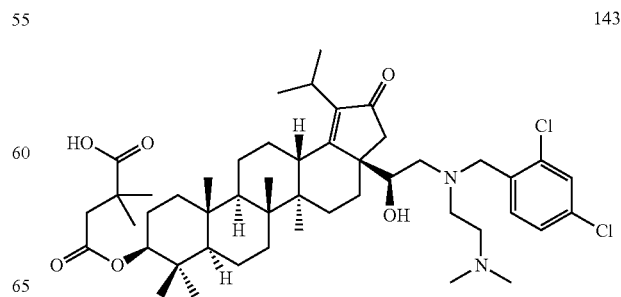


Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 751.5. found 752.3 (M+1)⁺.

Example 74

Compound 143

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((2,4-dichlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



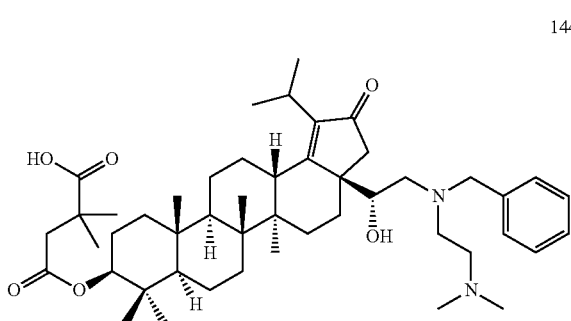
205

Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 842.5. found 843.3 (M+1)⁺.

Example 75

Compound 144

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(benzyl(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

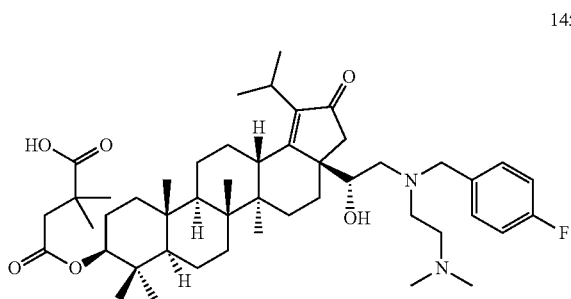


Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 774.6. found 775.4 (M+1)⁺.

Example 76

Compound 145

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-(dimethylamino)ethyl)(4-fluorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



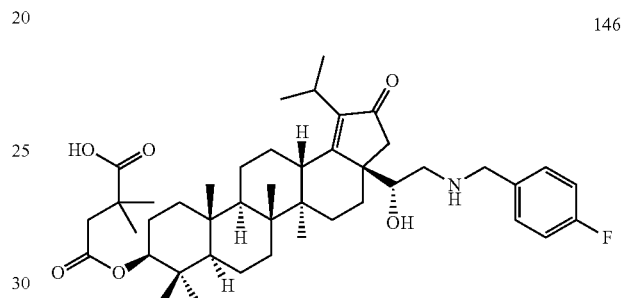
206

Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 792.5. found 793.5 (M+1)⁺.

Example 77

Compound 146

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-fluorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

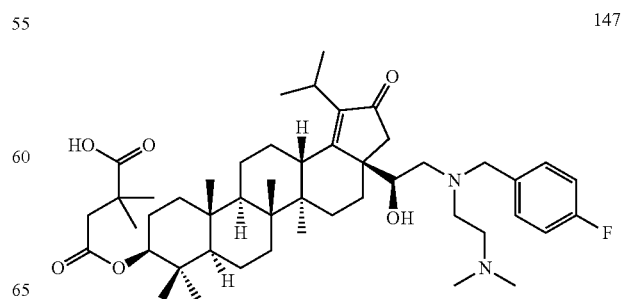


Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 721.5. found 722.3 (M+1)⁺.

Example 78

Compound 147

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((2-(dimethylamino)ethyl)(4-fluorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



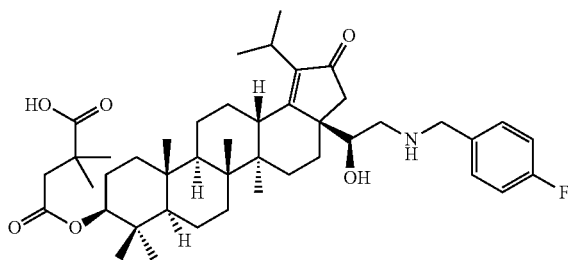
207

Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 792.5. found 793.5 (M+1)⁺.

Example 79

Compound 148

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-fluorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

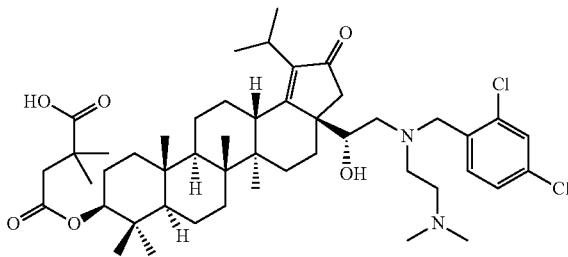


Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 721.5. found 722.3 (M+1)⁺.

Example 80

Compound 149

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2,4-dichlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



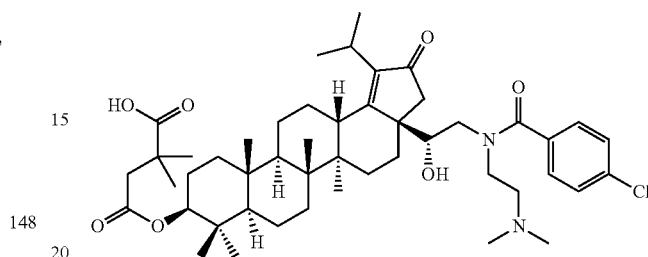
Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 842.5. found 843.5 (M+1)⁺.

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Example 81

Compound 150

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(4-chloro-N-(2-(dimethylamino)ethyl)benzamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

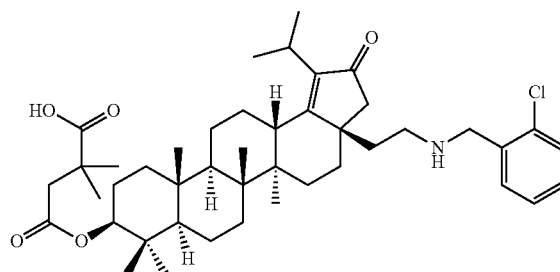


Stereochemistry was tentatively assigned as drawn but not fully confirmed spectroscopically. LC/MS: m/z calculated 822.5. found 823.4 (M+1)⁺.

Example 82

Compound 151

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((2-(2-chlorobenzyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

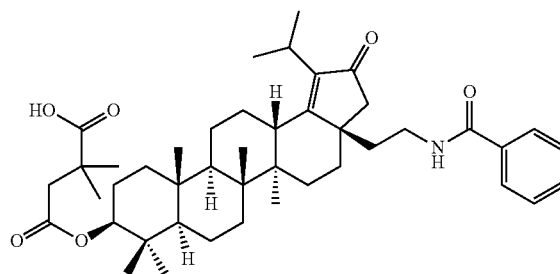


LC/MS: m/z calculated 721.5. found 722.3 (M+1)⁺.

Example 83

Compound 152

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((2-benzamidoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

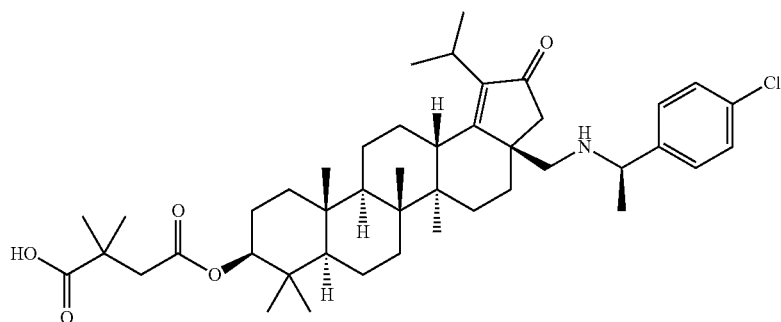


LC/MS: m/z calculated 701.5. found 702.5 (M+1)⁺.

Compound 153

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 (((R)-1-(4-Chlorophenyl)ethyl)amino)methyl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



153

LC/MS: m/z calculated 721.5. found 722.3 (M+1)⁺.

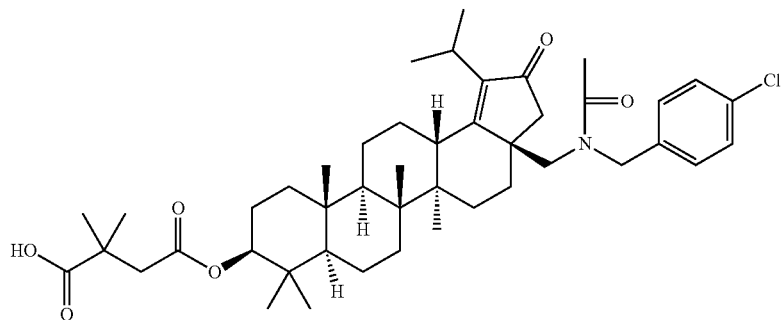
Example 85

35

Compound 154

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((N-
 (4-chlorobenzyl)acetamido)methyl)-1-isopropyl-5a,
 5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
 8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid

40



154

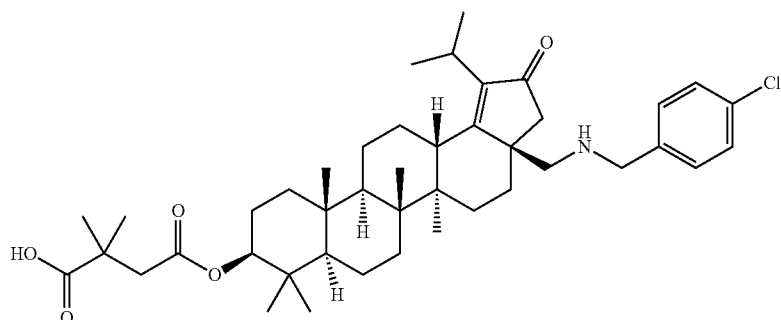
LC/MS: m/z calculated 749.4. found 750.3 (M+1)⁺.

Example 86

Compound 155

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(((4-chlorobenzyl)amino)methyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



155

LC/MS: m/z calculated 707.4. found 708.3 (M+1)⁺.

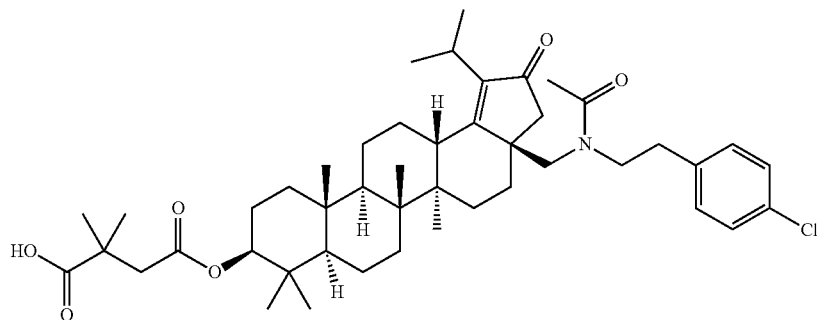
35

Example 87

Compound 156

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((N-(4-chlorophenethyl)acetamido)methyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



156

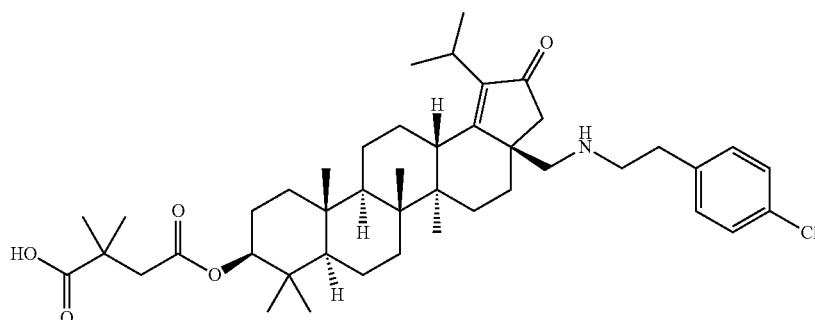
LC/MS: m/z calculated 763.5. found 764.3 (M+1)⁺.

Example 88

Compound 157

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(((4-chlorophenethyl)amino)methyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



157

LC/MS: m/z calculated 721.5. found 722.3 (M+1)⁺

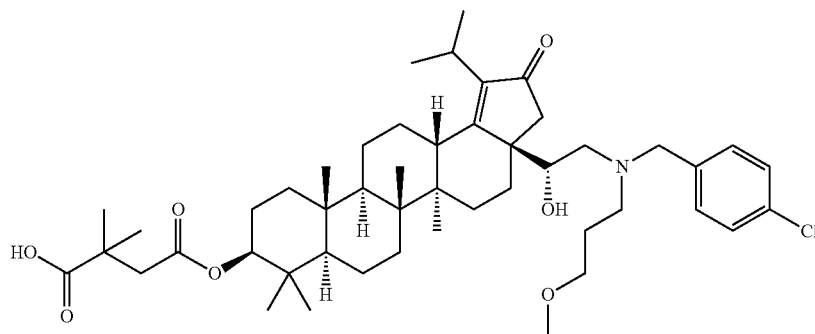
35

Example 89

Compound 158

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)(3-methoxypropyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



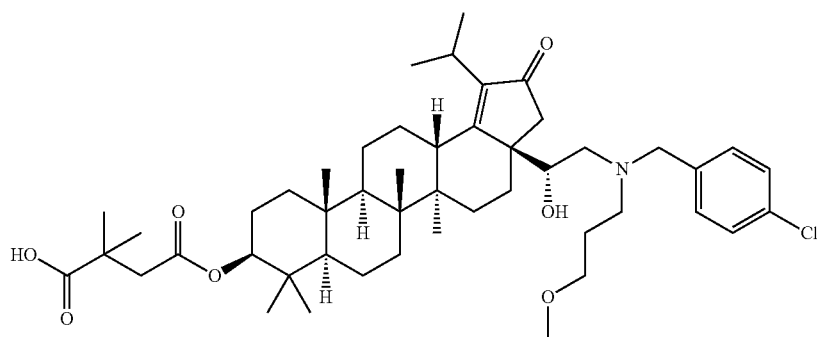
158

LC/MS: m/z calculated 809.50. found 810.7 (M+1)⁺

Compound 159

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)(3-methoxypropyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



159

LC/MS: m/z calculated 809.5. found 810.4 (M+1)⁺

35

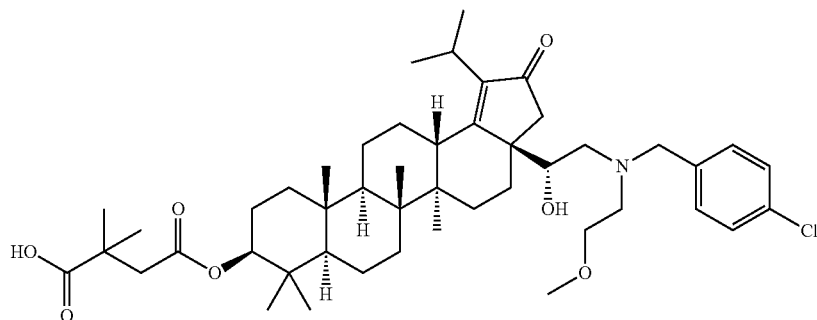
Example 91

Compound 160

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)(2-methoxyethyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



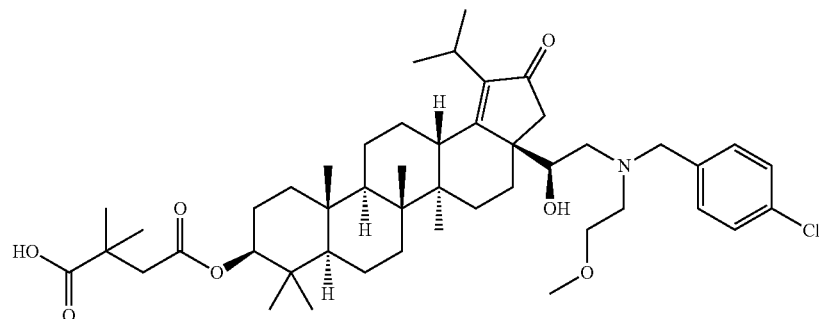
160

LC/MS: m/z calculated 795.5. found 796.3 (M+1)⁺

Compound 161

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)(2-methoxyethyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

5



161

LC/MS: m/z calculated 795.5. found 796.3 (M+1)⁺

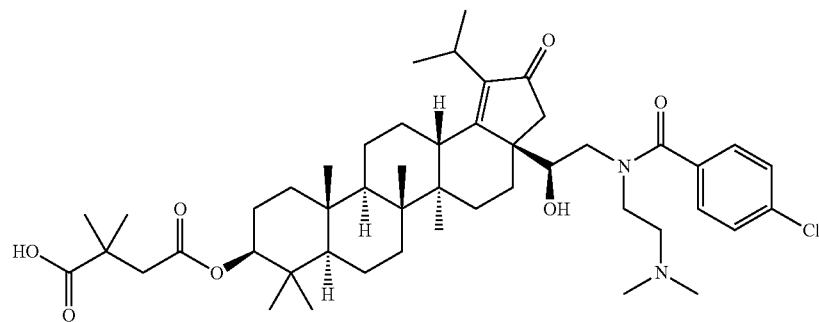
Example 93

35

Compound 162

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(4-chloro-N-(2-(dimethylamino)ethyl)benzamido)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



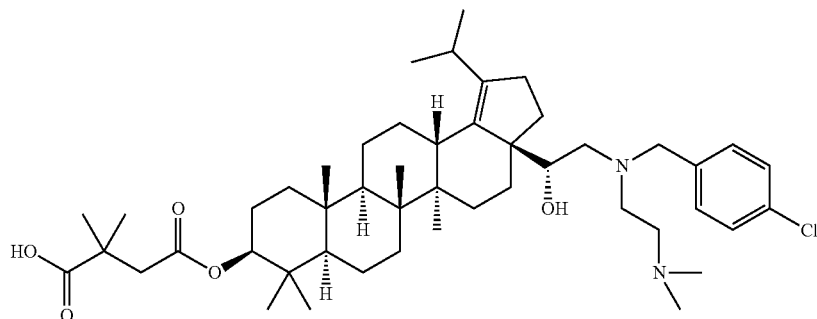
162

LC/MS: m/z calculated 822.5. found 823.5 (M+1)⁺

Compound 163

4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



163

LC/MS: m/z calculated 794.5. found 795.5 (M+1)⁺

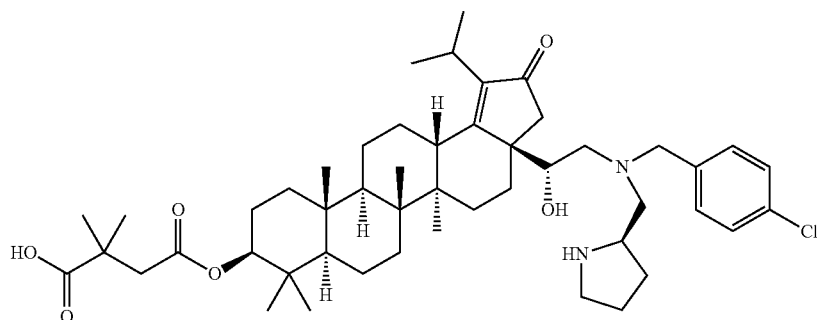
Example 95

35

Compound 164

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)((R)-pyrrolidin-2-ylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



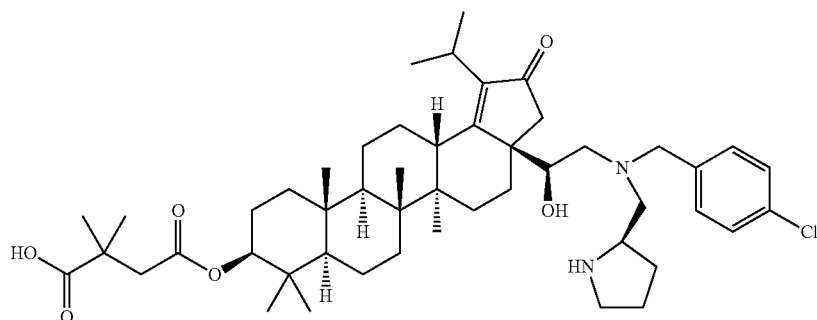
164

LC/MS: m/z calculated 820.5. found 821.5 (M+1)⁺

Compound 165

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)((R)-pyrrolidin-2-ylmethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



165

LC/MS: m/z calculated 820.5. found 821.5 (M+1)⁺

35

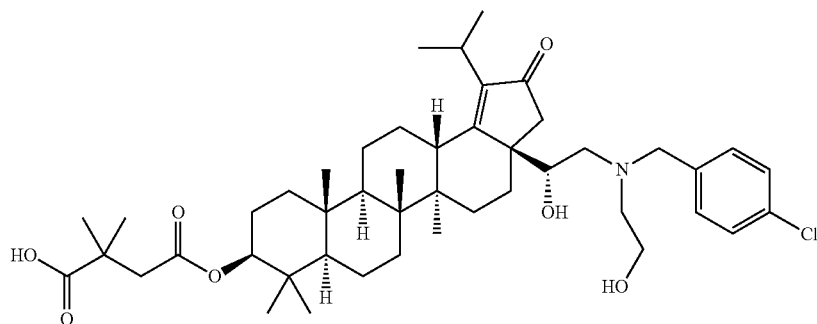
Example 97

Compound 166

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)(2-hydroxyethyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



166

LC/MS: m/z calculated 781.5. found 782.5 (M+1)⁺

223

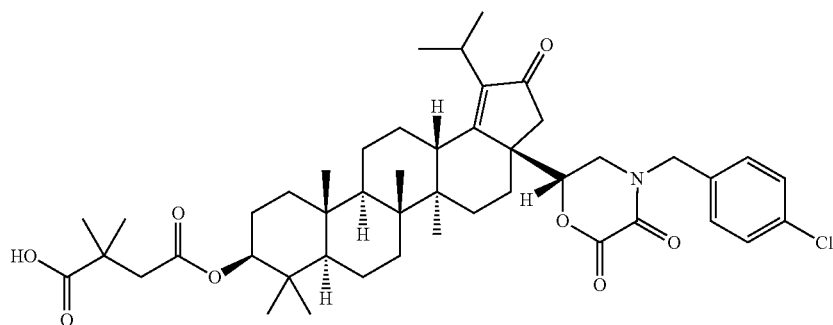
Example 98

224

Compound 167

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-4-(4-chlorobenzyl)-5,6-dioxomorpholin-2-yl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



167

LC/MS: m/z calculated 791.4. found 792.5 (M+1)⁺

35

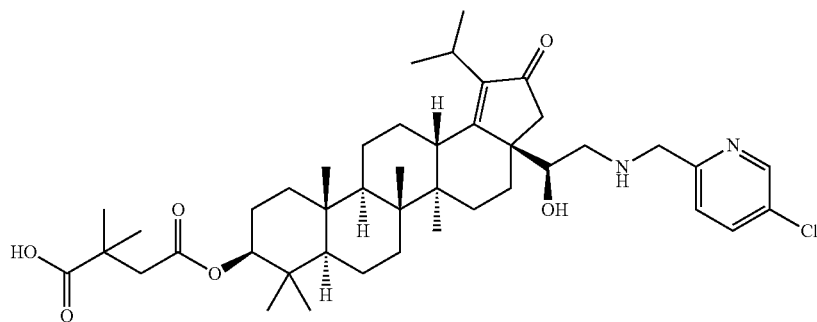
Example 99

Compound 168

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(((5-chloropyridin-2-yl)methyl)amino)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



168

LC/MS: m/z calculated 738.4. found 739.5 (M+1)⁺

225

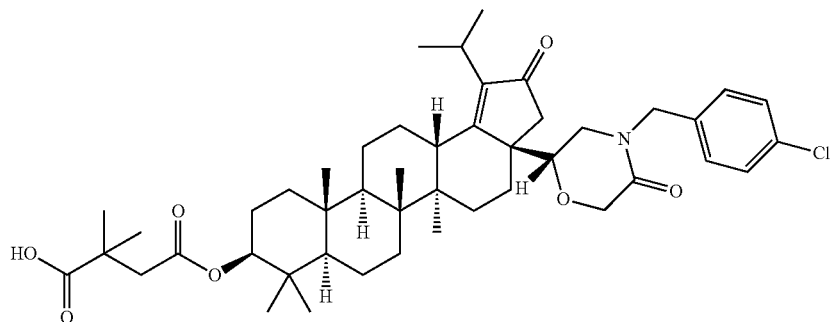
Example 100

226

Compound 169

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-4-(4-chlorobenzyl)-5-oxomorpholin-2-yl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



169

LC/MS: m/z calculated 777.4. found 778.6 (M+1)⁺

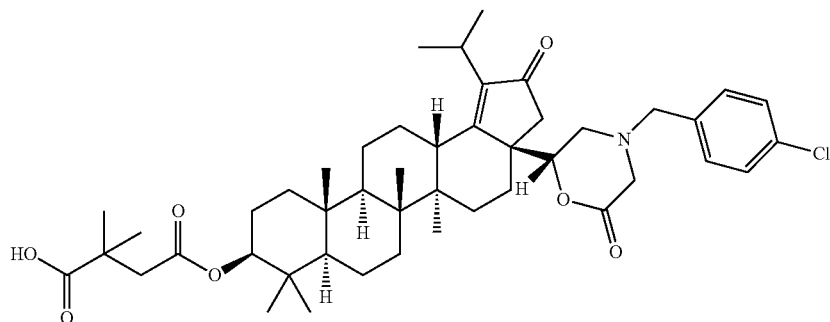
Example 101

35

Compound 170

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-4-(4-chlorobenzyl)-6-oxomorpholin-2-yl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40



170

LC/MS: m/z calculated 777.4. found 777.9 (M+1)⁺

227

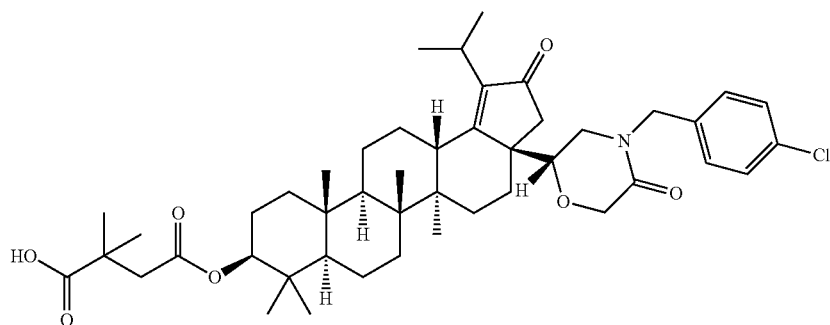
Example 102

228

Compound 171

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
4-(4-chlorobenzyl)-5-oxomorpholin-2-yl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5



171

LC/MS: m/z calculated 777.4. found 777.9 (M+1)⁺

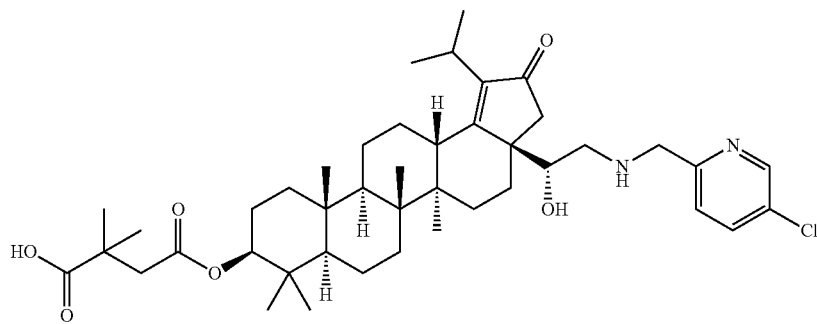
Example 103

35

Compound 172

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((5-chloropyridin-2-yl)methyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



172

LC/MS: m/z calculated 737.4. found 739.4 (M+1)⁺

229

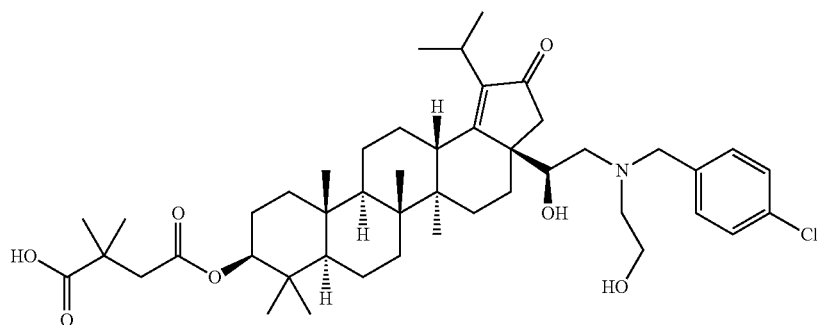
230

Example 104

Compound 173

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)(2-hydroxyethyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

5



173

LC/MS: m/z calculated 781.5. found 782.3 (M+1)⁺

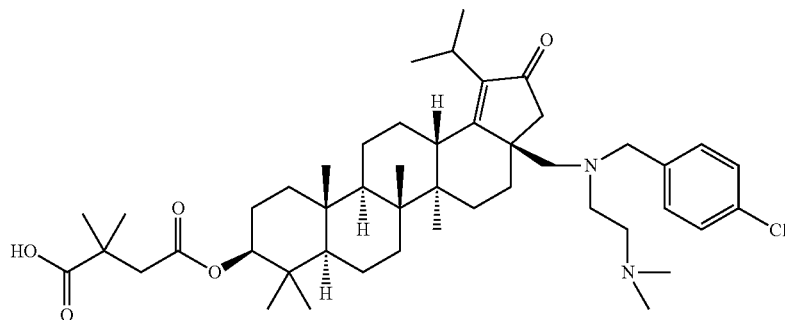
Example 105

35

Compound 174

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(((4-
chlorobenzyl)(2-(dimethylamino)ethyl)amino)me-
thyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40



174

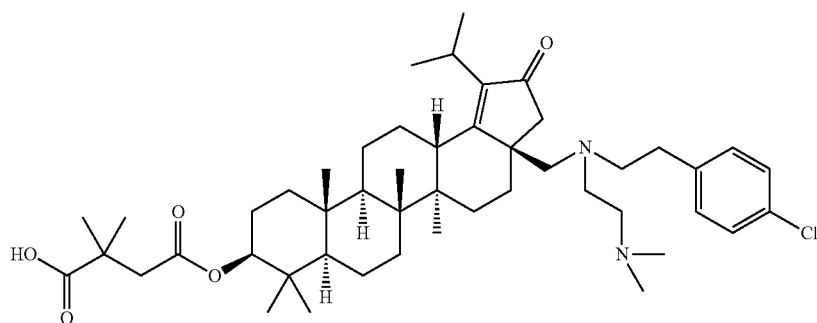
LC/MS: m/z calculated 778.5. found 779.5 (M+1)⁺

Example 106

Compound 175

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(((4-chlorophenethyl)(2-(dimethylamino)ethyl)amino)methyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



175

LC/MS: m/z calculated 792.5. found 793.5 (M+1)⁺

35

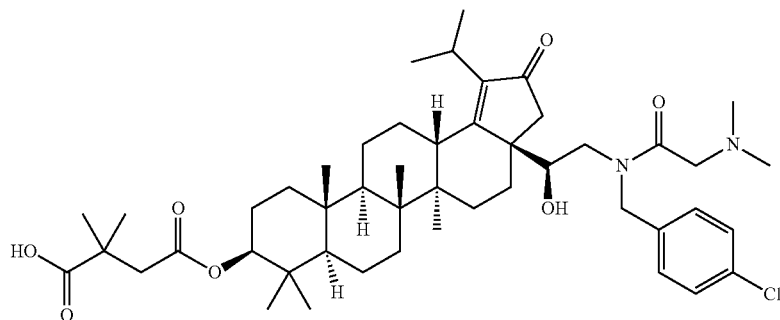
Example 107

Compound 176

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-(N-(4-chlorobenzyl)-2-(dimethylamino)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



176

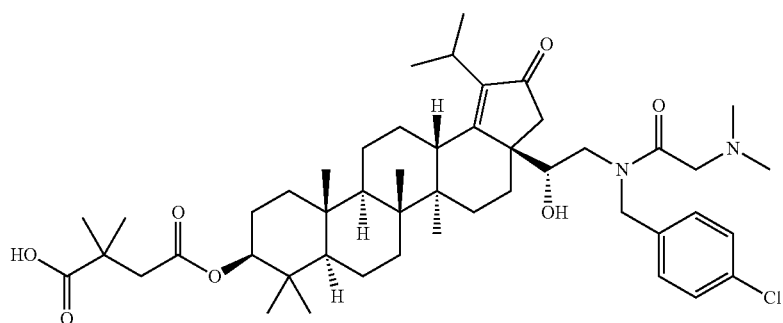
LC/MS: m/z calculated 822.5. found 823.5 (M+1)⁺

Example 108

Compound 177

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(4-chlorobenzyl)-2-(dimethylamino)aceta-
mido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



177

LC/MS: m/z calculated 822.5. found 823.5 (M+1)⁺

35

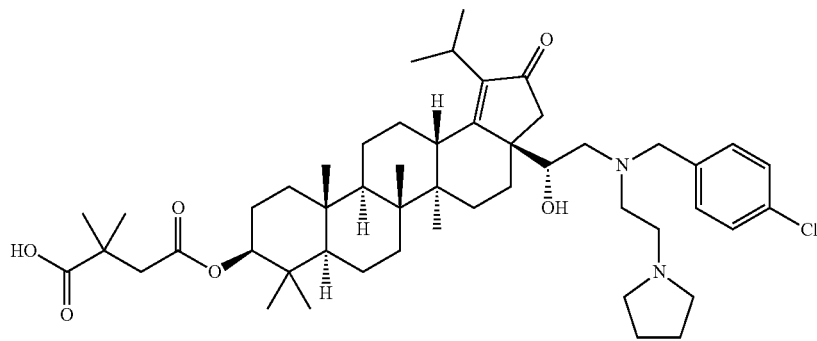
Example 109

Compound 178

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)(2-(pyrrolidin-1-yl)ethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



178

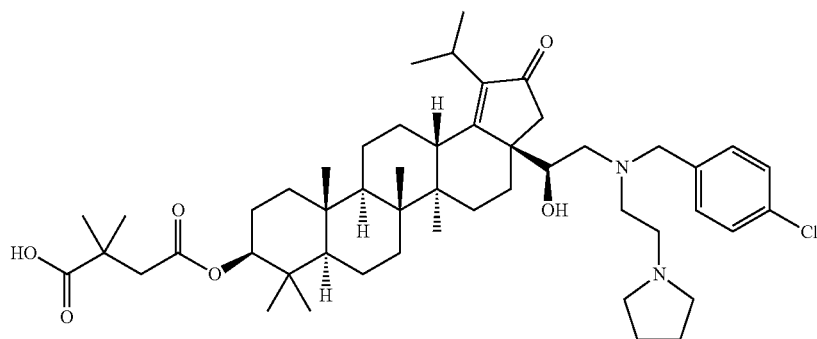
LC/MS: m/z calculated 834.5. found 835.5 (M+1)⁺

Example 110

Compound 179

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)(2-(pyrrolidin-1-yl)ethyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



179

LC/MS: m/z calculated 834.5. found 835.5 (M+1)⁺

35

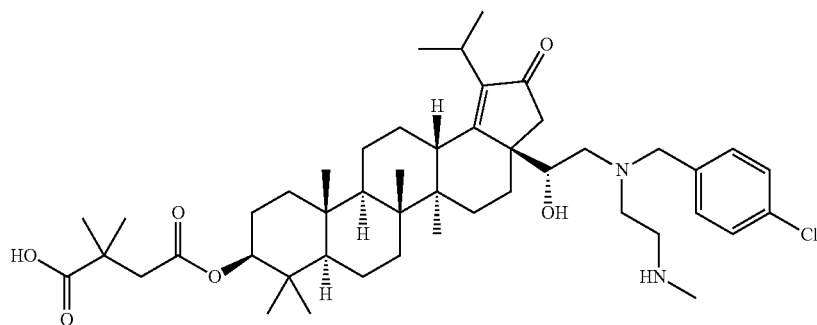
Example 111

Compound 180

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)(2-(methylamino)ethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



180

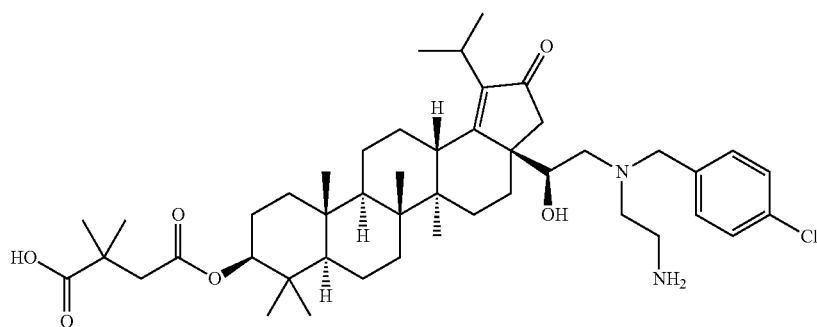
LC/MS: m/z calculated 794.5. found 795.4 (M+1)⁺

Example 112

Compound 181

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((2-aminoethyl)(4-chlorobenzyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

5



181

LC/MS: m/z calculated 780.5. found 781.4 (M+1)⁺

35

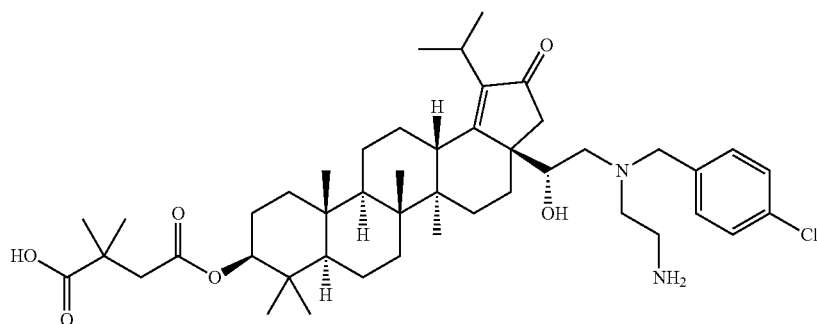
Example 113

Compound 182

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-aminoethyl)(4-chlorobenzyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



182

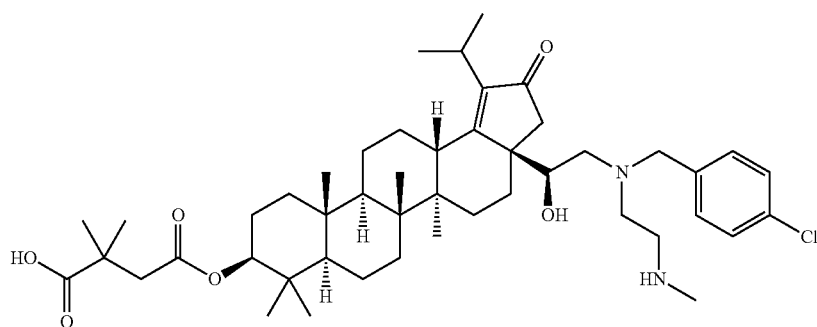
LC/MS: m/z calculated 780.5. found 781.4 (M+1)⁺

Example 114

Compound 183

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)(2-(methylamino)ethyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



183

LC/MS: m/z calculated 794.5. found 795.5 (M+1)⁺

35

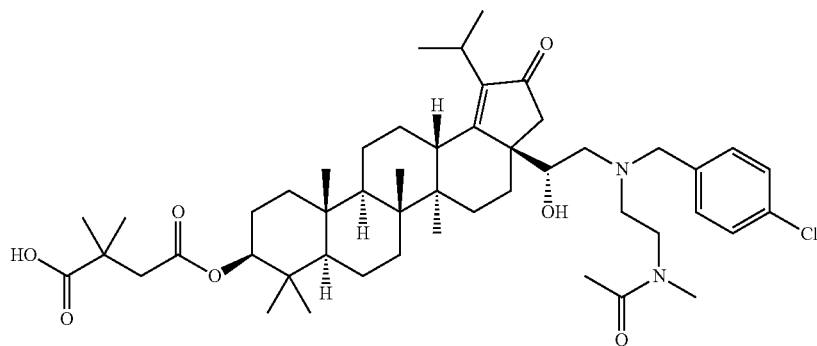
Example 115

Compound 184

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)(2-(N-methylacetamido)
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

40

45



184

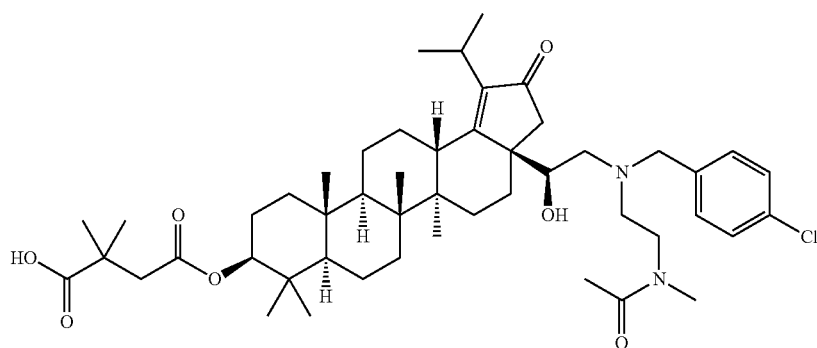
LC/MS: m/z calculated 836.5. found 837.5 (M+1)⁺

Example 116

Compound 185

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)(2-(N-methylacetamido)ethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



185

LC/MS: m/z calculated 836.5. found 837.5 (M+1)⁺

35

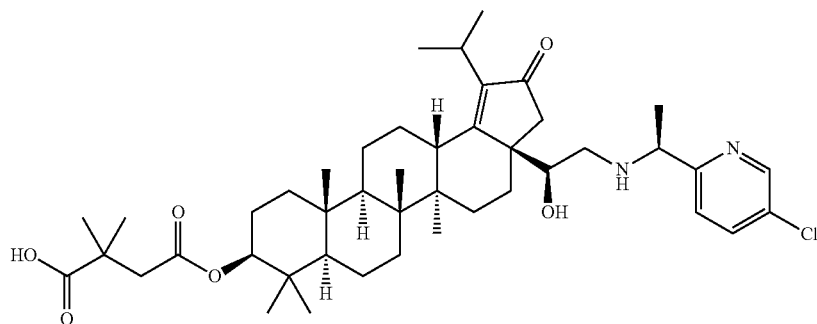
Example 117

Compound 186

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(((S)-1-(5-chloropyridin-2-yl)ethyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



186

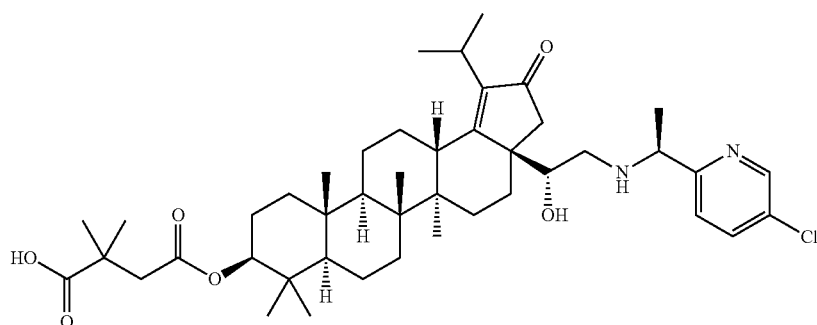
LC/MS: m/z calculated 752.5. found 753.4 (M+1)⁺

Example 118

Compound 187

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((S)-1-(5-chloropyridin-2-yl)ethyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



187

LC/MS: m/z calculated 752.5. found 753.4 (M+1)⁺

35

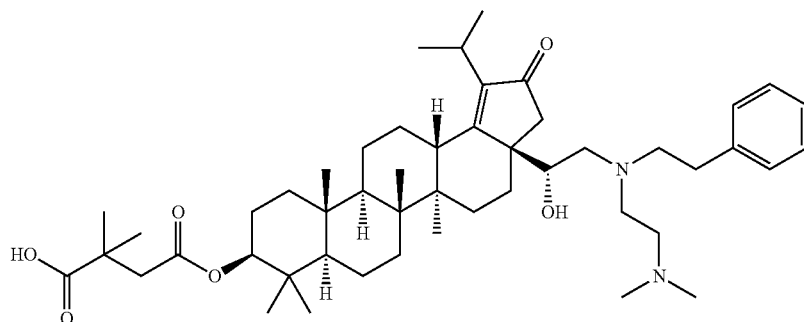
Example 119

Compound 188

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(phenethyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



188

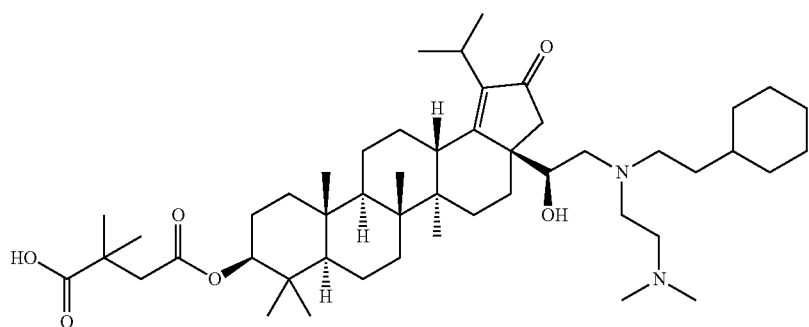
LC/MS: m/z calculated 788.6. found 789.5 (M+1)⁺

Example 120

Compound 189

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(cyclohexyl(2-(dimethylamino)ethyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



189

LC/MS: m/z calculated 766.6. found 767.6 (M+1)⁺

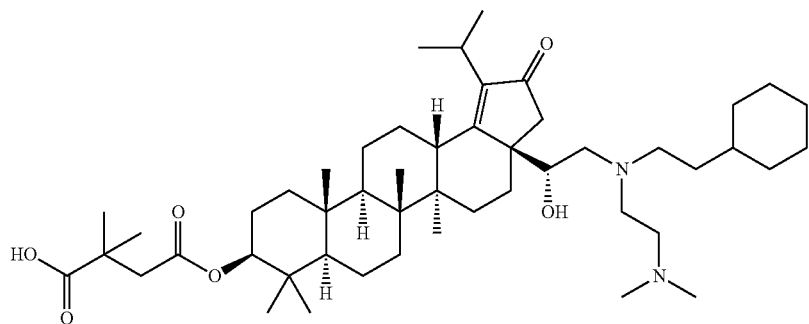
35

Example 121

Compound 190

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(cyclohexyl(2-(dimethylamino)ethyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



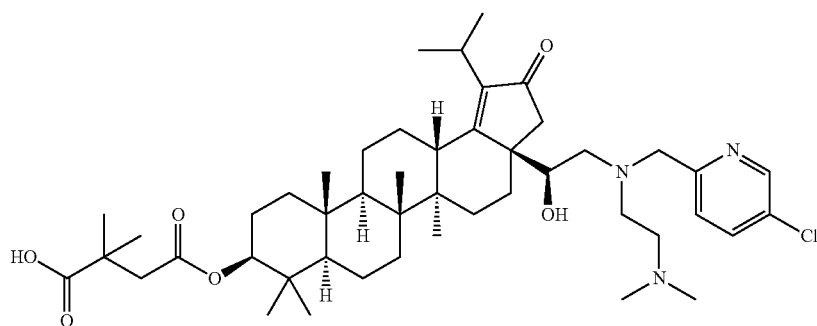
190

LC/MS: m/z calculated 766.6. found 767.6 (M+1)⁺

Example 122

Compound 191

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(((5-chloropyridin-2-yl)methyl)(2-(dimethyl-
lamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 5 10



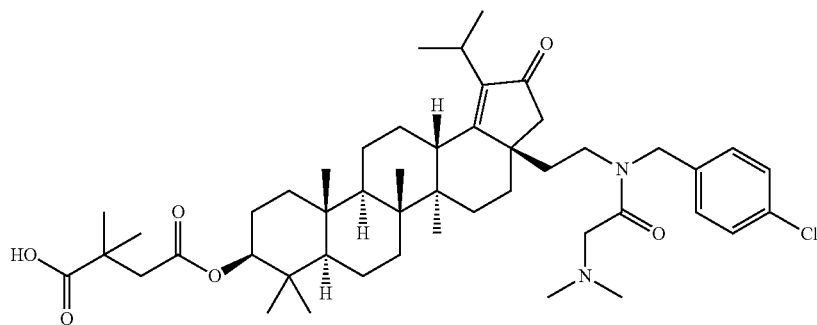
191

LC/MS: m/z calculated 809.5. found 810.5 (M+1)⁺ 35

Example 123

Compound 192

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(N-(4-chlorobenzyl)-2-(dimethylamino)acetamido)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid 40 45



192

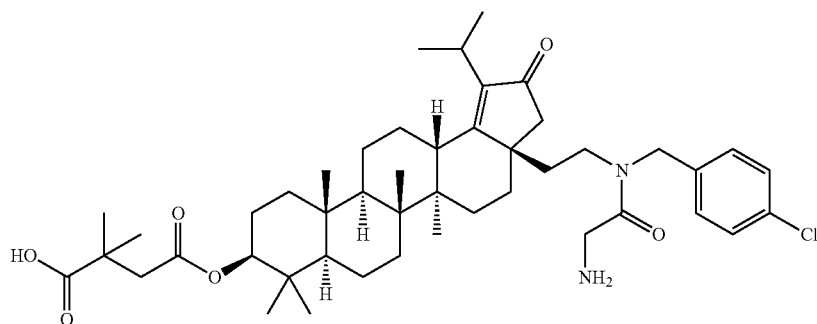
LC/MS: m/z calculated 806.5. found 807.4 (M+1)⁺

Example 124

Compound 193

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(2-amino-N-(4-chlorobenzyl)acetamido)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



193

LC/MS: m/z calculated 778.5. found 779.4 (M+1)⁺

35

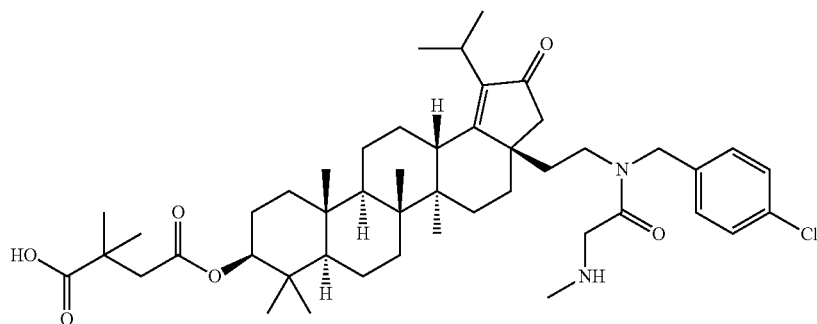
Example 125

Compound 194

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(N-(4-chlorobenzyl)-2-(methylamino)acetamido)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



194

LC/MS: m/z calculated 792.5. found 793.4 (M+1)⁺

251

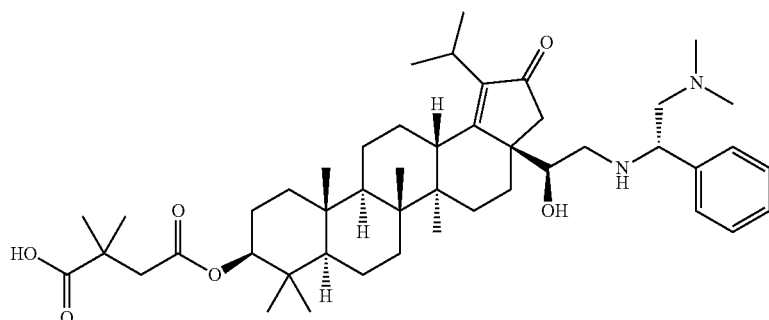
Example 126

252

Compound 195

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(((S)-2-(dimethylamino)-1-phenylethyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



195

LC/MS: m/z calculated 760.5. found 761.5 (M+1)⁺

35

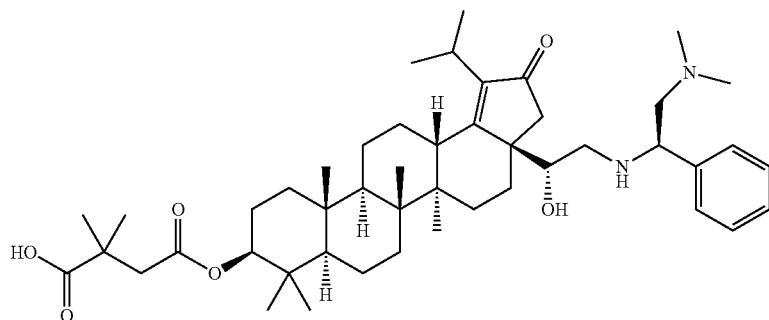
Example 127

Compound 196

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((R)-2-(dimethylamino)-1-phenylethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



196

LC/MS: m/z calculated 760.5. found 761.5 (M+1)⁺

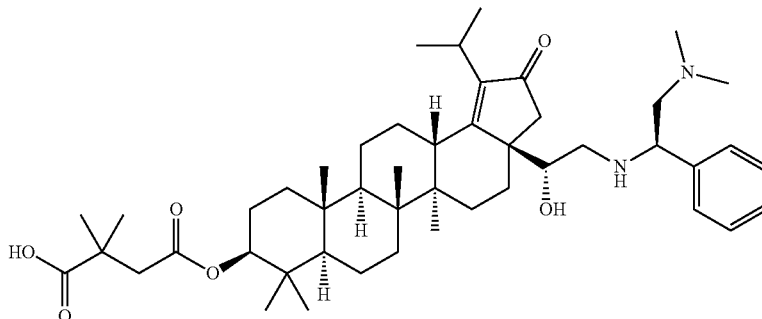
Example 128

Compound 197

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((R)-2-(dimethylamino)-1-phenylethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5

197



30

LC/MS: m/z calculated 760.5. found 761.5 (M+1)⁺

Example 129

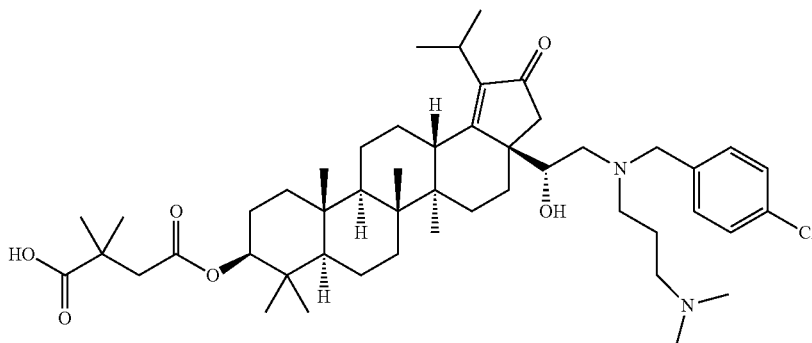
Compound 198

35

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)(3-(dimethylamino)propyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

198



LC/MS: m/z calculated 822.5. found 823.5 (M+1)⁺

255

Example 130

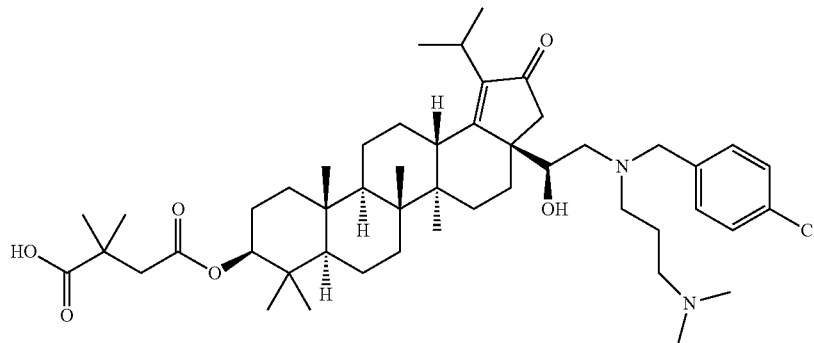
Compound 199

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)(3-(dimethylamino)propyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5

256

199



LC/MS: m/z calculated 822.5. found 823.5 (M+1)⁺

Example 132

Example 131

35

Compound 201

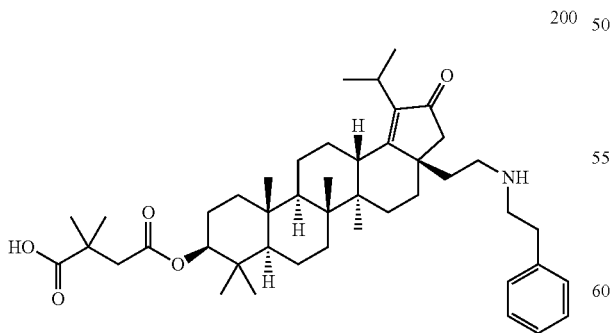
Compound 200

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-
(phenethylamino)ethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(isopropyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

45



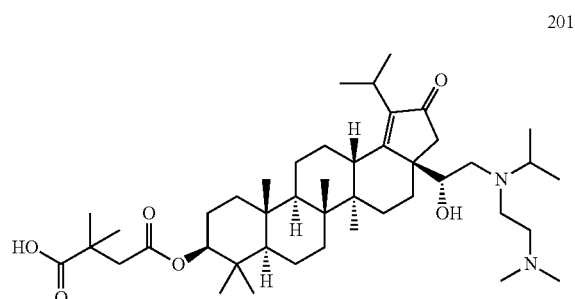
200 50

55

60

65

LC/MS: m/z calculated 701.5. found 702.5 (M+1)⁺



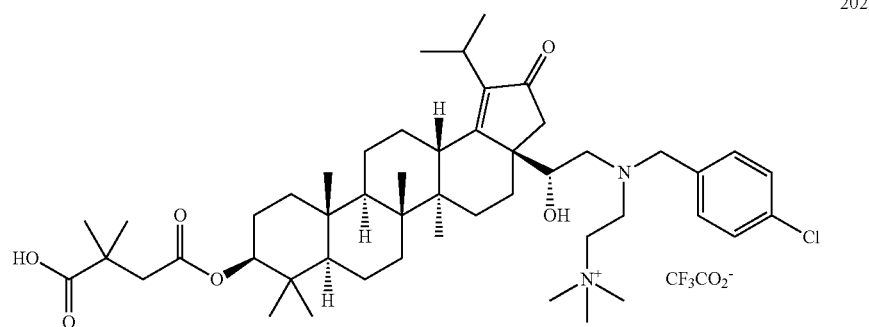
201

LC/MS: m/z calculated 726.5. found 727.5 (M+1)⁺

Example 133

Compound 202

2-(((R)-2-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-
9-((3-carboxy-3-methylbutanoyl)oxy)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-3a-yl)-2-hydroxyethyl)(4-
chlorobenzyl)amino)-N,N,N-trimethylethanaminium
trifluoroacetate 5 10

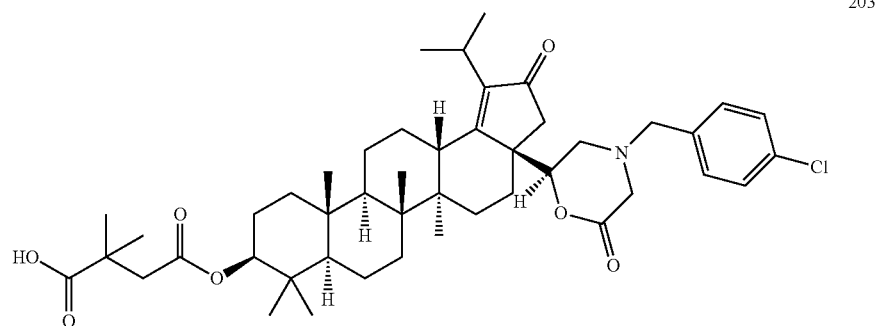


LC/MS: m/z calculated 823.5. found 823.5 (M)⁺ 35

Example 134

Compound 203

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
4-(4-chlorobenzyl)-6-oxomorpholin-2-yl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 40 45



LC/MS: m/z calculated 777.4. found 778.4 (M+1)⁺

259

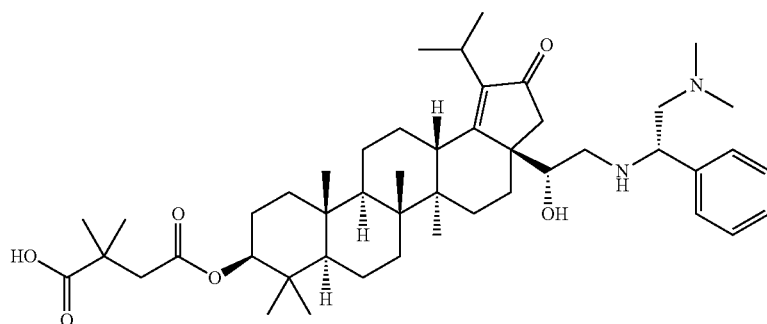
260

Example 135

Compound 204

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(((S)-2-(dimethylamino)-1-phenylethyl)
 amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
 pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
 11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
 chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



204

LC/MS: m/z calculated 760.5. found 761.4 (M+1)⁺

Example 136

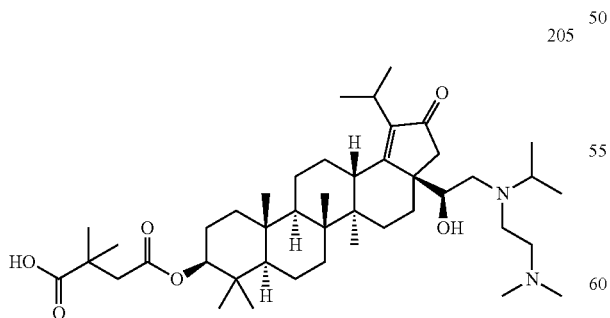
35

Compound 205

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
 2-((2-(dimethylamino)ethyl)(isopropyl)amino)-1-
 hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45

50
205

55

60

65

LC/MS: m/z calculated 726.6. found 727.5 (M+1)⁺

261

Example 137

262

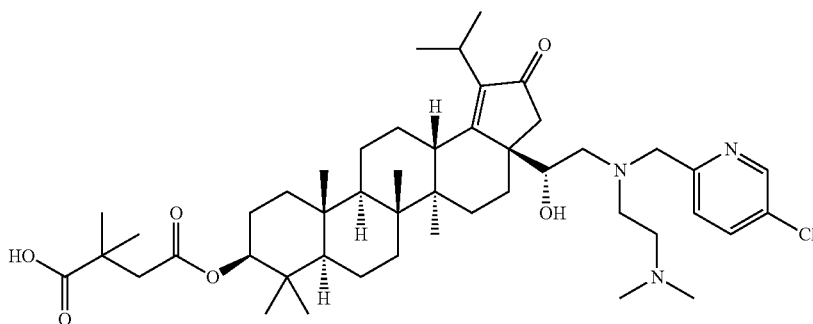
Compound 206

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((5-chloropyridin-2-yl)methyl)(2-(dimethyl-
amino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

10

206



LC/MS: m/z calculated 809.5. found 810.5 (M+1)⁺

Example 138

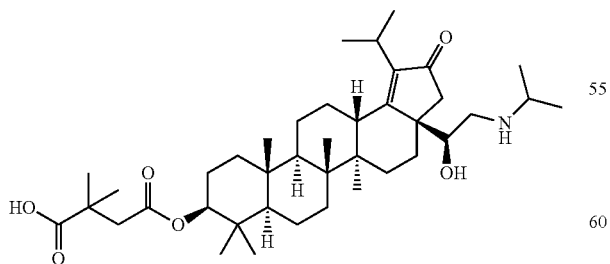
35

Compound 207

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(isopropylamino)ethyl)-1-isopropyl-5a,
5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

45

50
207

55

60

65

LC/MS: m/z calculated 655.5. found 656.4 (M+1)⁺

263

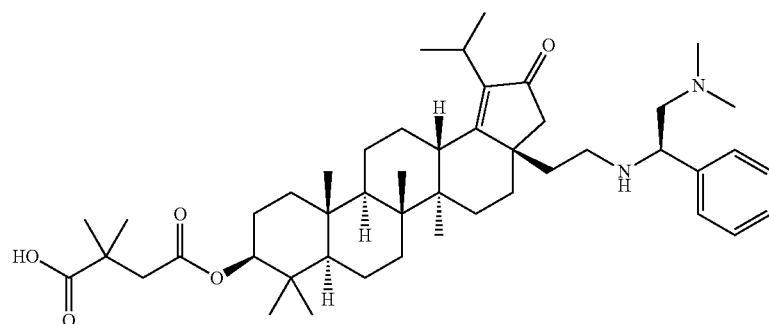
Example 139

264

Compound 208

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 (((R)-2-(dimethylamino)-1-phenylethyl)amino)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



208

LC/MS: m/z calculated 744.5. found 745.5 (M+1)⁺

35

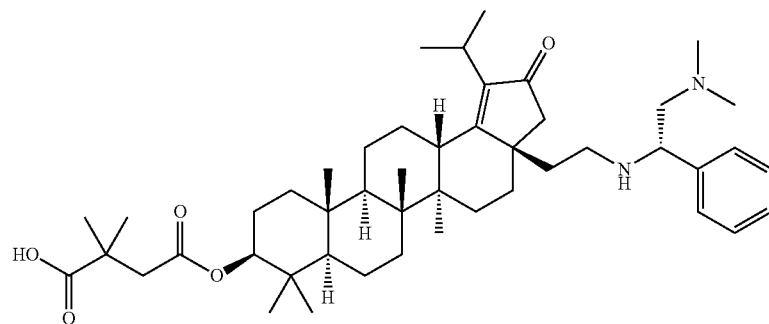
Example 140

Compound 209

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 (((S)-2-(dimethylamino)-1-phenylethyl)amino)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40

45



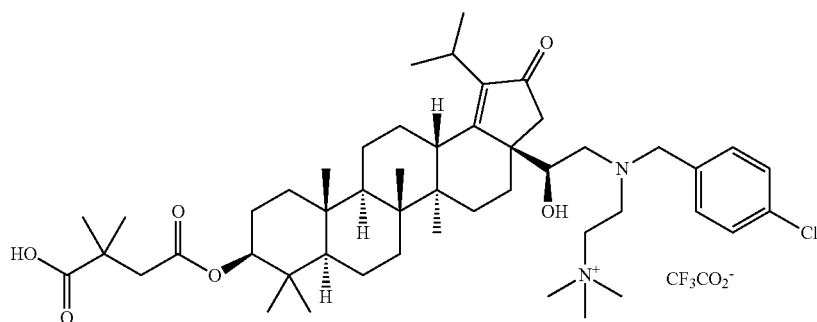
209

LC/MS: m/z calculated 744.5. found 745.5 (M+1)⁺

Example 141

Compound 210

2-(((S)-2-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-
9-((3-carboxy-3-methylbutanoyl)oxy)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-3a-yl)-2-hydroxyethyl)(4-
chlorobenzyl)amino)-N,N,N-trimethylethanaminium
trifluoroacetate 5 10



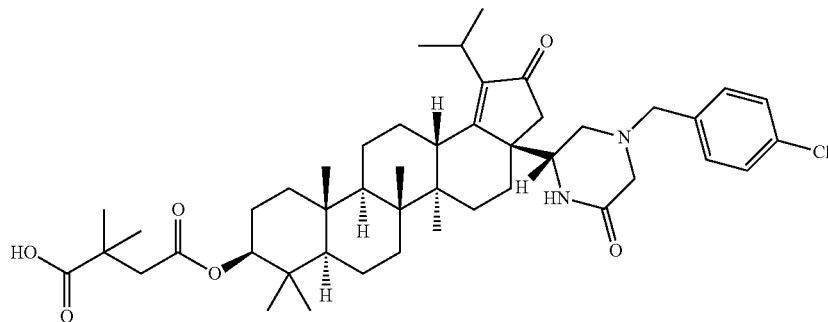
210

LC/MS: m/z calculated 823.5. found 823.5 (M)⁺ 35

Example 142

Compound 211

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-4-(4-chlorobenzyl)-6-oxopiperazin-2-yl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid 40 45



211

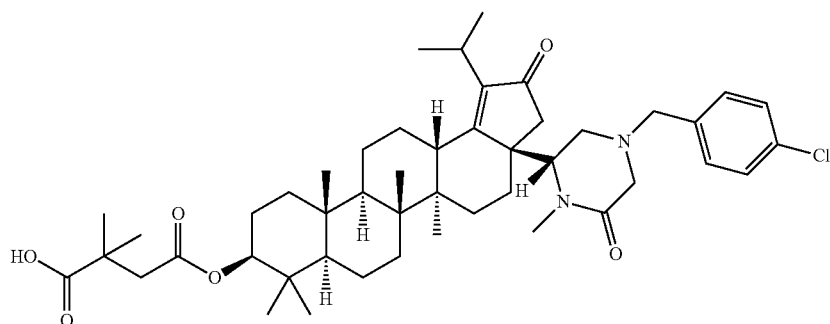
LC/MS: m/z calculated 776.5. found 777.4 (M+1)⁺

Example 143

Compound 212

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
4-(4-chlorobenzyl)-1-methyl-6-oxopiperazin-2-yl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



212

LC/MS: m/z calculated 790.5. found 791.4 (M+1)⁺

35

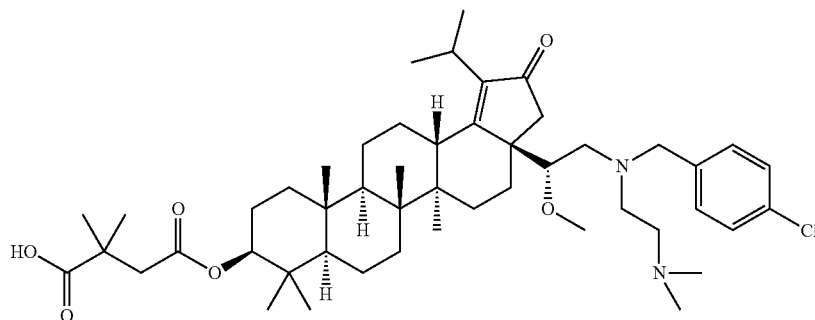
Example 144

Compound 213

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)
amino)-1-methoxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



213

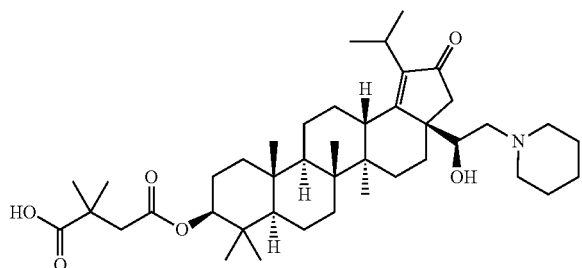
LC/MS: m/z calculated 822.5. found 823.5 (M+1)⁺

269

Example 145

Compound 214

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-hydroxy-2-(piperidin-1-yl)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



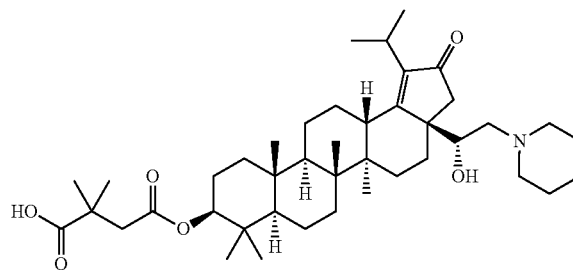
LC/MS: m/z calculated 681.5. found 682.5 (M+1)⁺

270

Example 146

Compound 215

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-hydroxy-2-(piperidin-1-yl)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

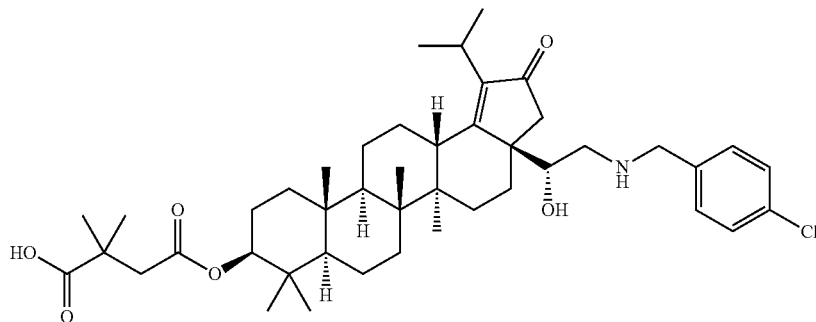


LC/MS: m/z calculated 681.5. found 682.5 (M+1)⁺

Example 147

Compound 216

4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



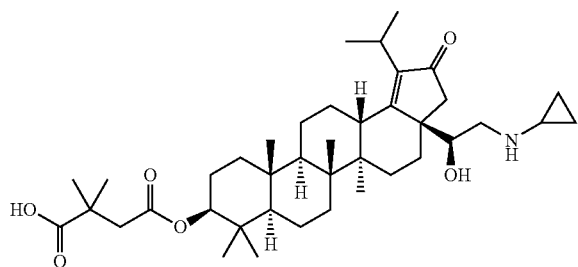
LC/MS: m/z calculated 723.5. found 724.4 (M+1)⁺

271

Example 148

Compound 217

4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



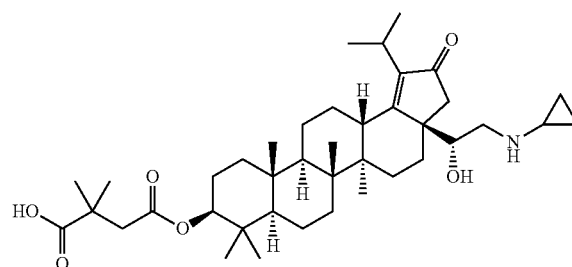
LC/MS: m/z calculated 653.5. found 654.4 (M+1)⁺

272

Example 149

Compound 218

4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

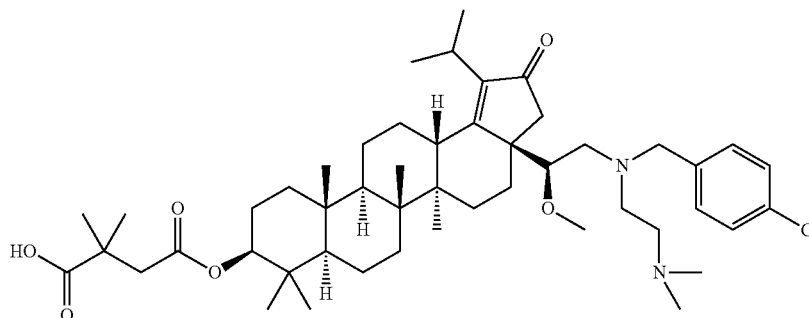


LC/MS: m/z calculated 653.5. found 654.4 (M+1)⁺

Example 150

Compound 219

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-methoxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 822.5. found 823.5 (M+1)⁺

273

274

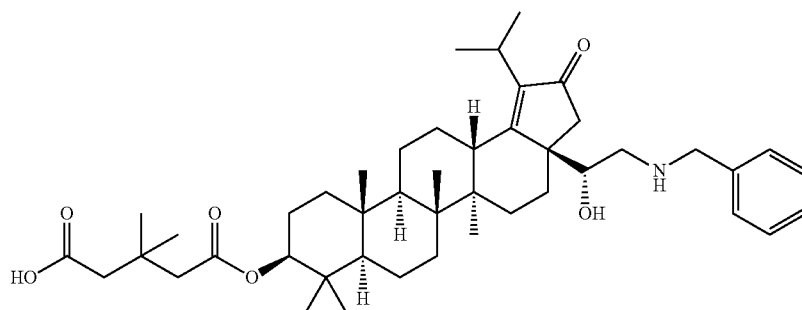
Example 151

Compound 220

5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(benzylamino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-3,3-dimethyl-5-
oxopentanoic acid

5

220



LC/MS: m/z calculated 717.5. found 718.5 (M+1)⁺

35

Example 152

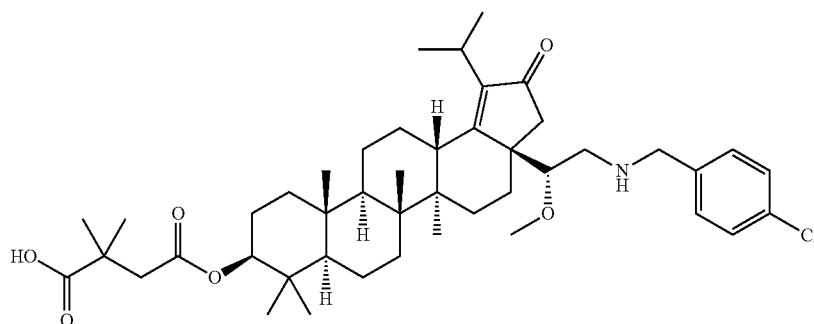
Compound 221

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)amino)-1-methoxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45

221



LC/MS: m/z calculated 751.5. found 752.5 (M+1)⁺

275

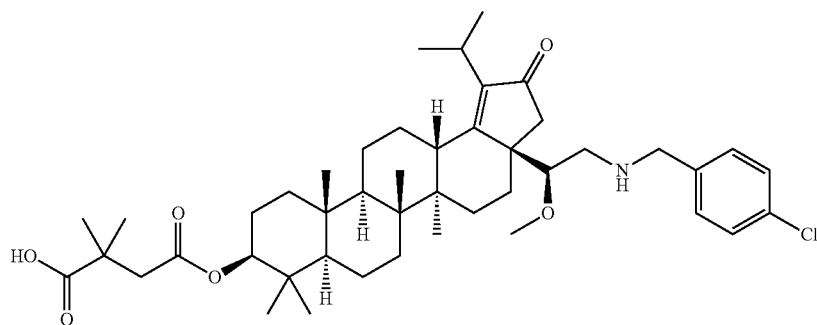
Example 153

276

Compound 222

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)amino)-1-methoxyethyl)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



222

LC/MS: m/z calculated 751.5. found 752.5 (M+1)⁺

35

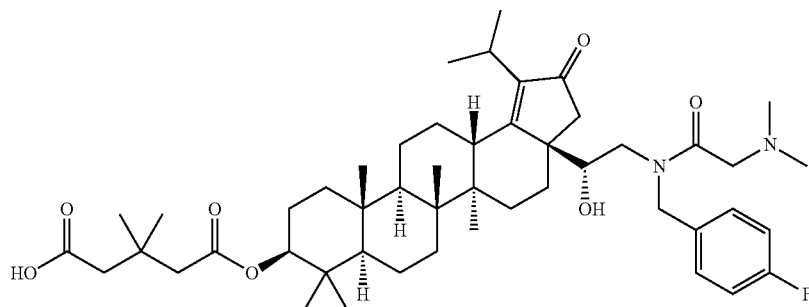
Example 154

Compound 223

5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-(dimethylamino)-N-(4-fluorobenzyl)aceta-
mido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid

40

45



223

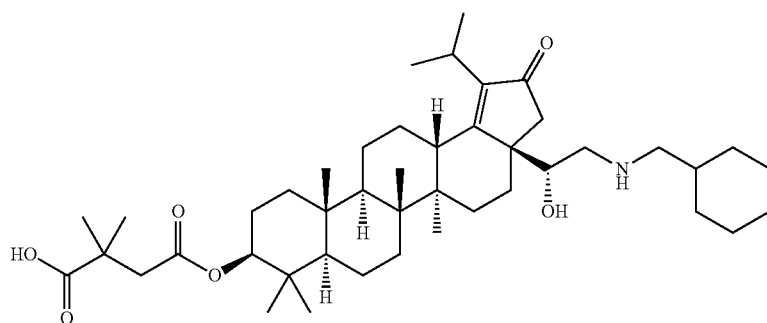
LC/MS: m/z calculated 820.5. found 821.5 (M+1)⁺

Example 155

Compound 224

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((cyclohexylmethyl)amino)-1-hydroxyethyl)-
 1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
 5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



224

LC/MS: m/z calculated 709.5. found 710.6 (M+1)⁺

35

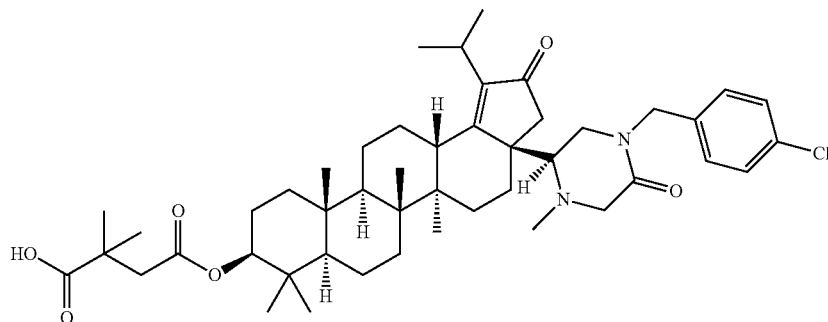
Example 156

Compound 225

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
 4-(4-chlorobenzyl)-1-methyl-5-oxopiperazin-2-yl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40

45



225

LC/MS: m/z calculated 790.5. found 791.5 (M+1)⁺

279

280

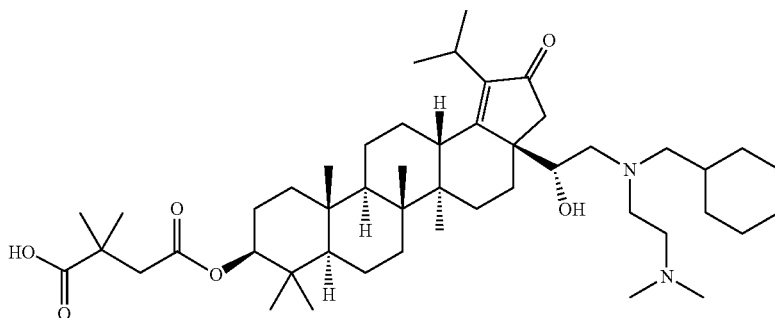
Example 157

Compound 226

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((cyclohexylmethyl)(2-(dimethylamino)ethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5

226



LC/MS: m/z calculated 780.6. found 781.5 (M+1)⁺

Example 158

35

Compound 227

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((cyclopropylmethyl)(2-(dimethylamino)
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

40

45

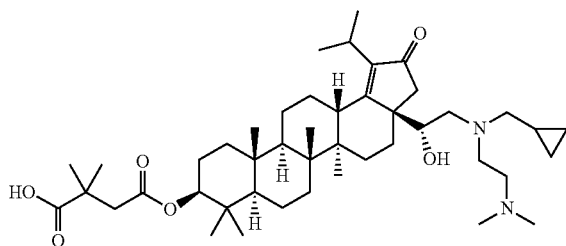
50

227

55

60

65



LC/MS: m/z calculated 738.6. found 739.8 (M+1)⁺

281

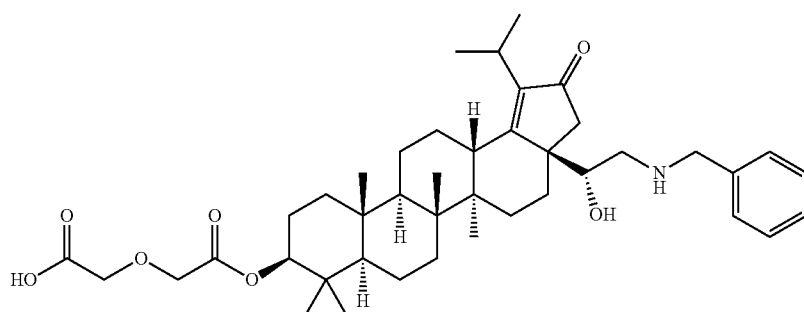
282

Example 159

Compound 228

2-(2-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(benzylamino)-1-hydroxyethyl)-1-isopropyl-
 5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
 7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2-oxoethoxy)acetic
 acid

5



228

LC/MS: m/z calculated 691.4. found 692.5 (M+1)⁺

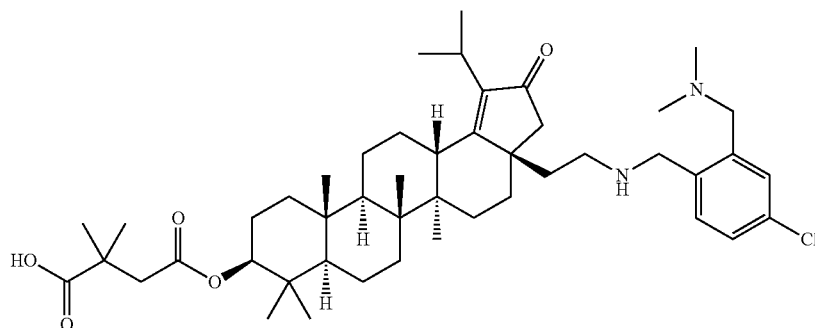
Example 160

35

Compound 229

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((4-chloro-2-((dimethylamino)methyl)benzyl)amino)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40



229

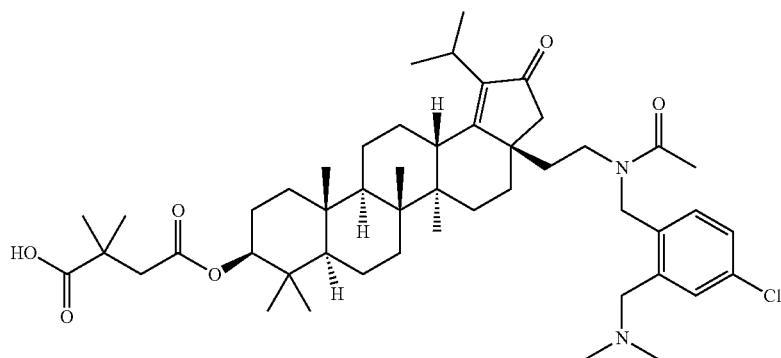
LC/MS: m/z calculated 778.5. found 779.5 (M+1)⁺

Example 161

Compound 230

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(N-(4-chloro-2-((dimethylamino)methyl)benzyl)
acetamido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



230

LC/MS: m/z calculated 820.5. found 821.7 (M+1)⁺

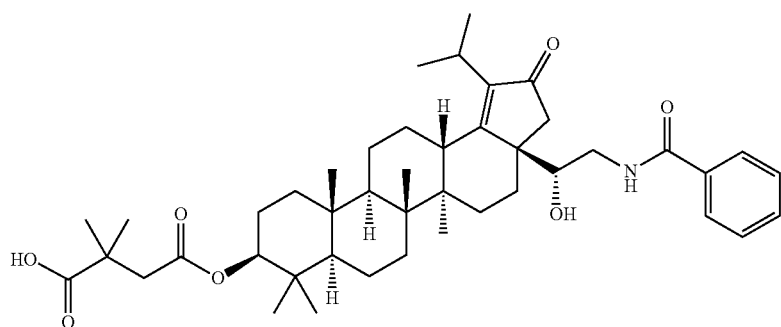
Example 162

Compound 231

40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(N-(4-chloro-2-((dimethylamino)methyl)benzyl)
acetamido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

45



231

LC/MS: m/z calculated 717.5. found 718.5 (M+1)⁺

285

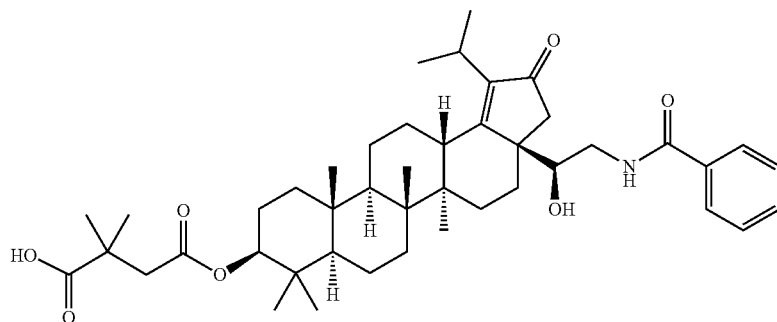
286

Example 163

Compound 232

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-benzamido-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

5



232

LC/MS: m/z calculated 717.5. found 718.5 (M+1)⁺

35

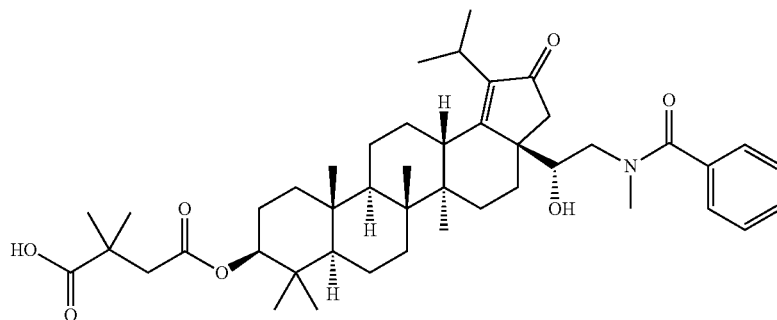
Example 164

Compound 233

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-methylbenzamido) ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



233

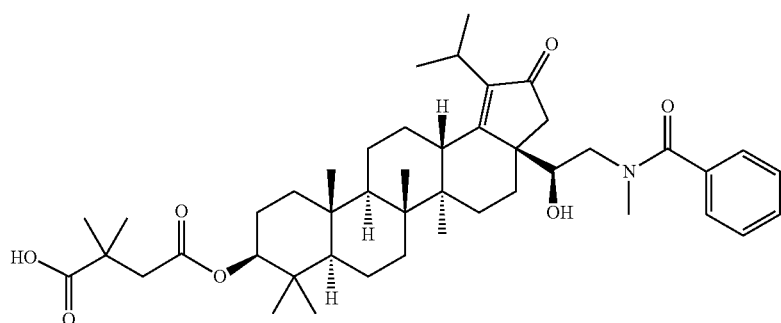
LC/MS: m/z calculated 731.5. found 732.3 (M+1)⁺

Example 165

Compound 234

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(N-methylbenzamido)ethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5



234

LC/MS: m/z calculated 731.5. found 732.5 (M+1)⁺

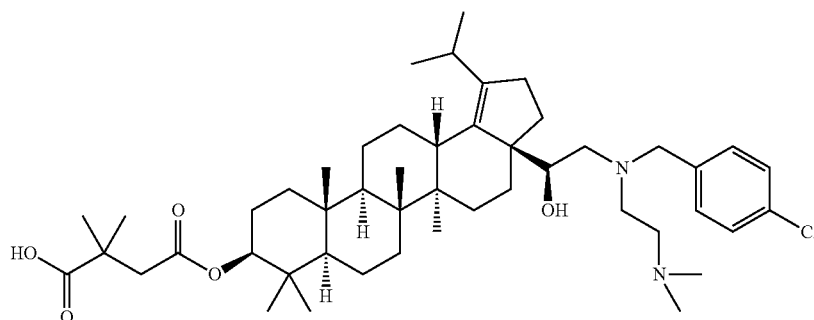
Example 166

35

Compound 235

4-(((3aS,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

40



235

LC/MS: m/z calculated 794.5. found 795.7 (M+1)⁺

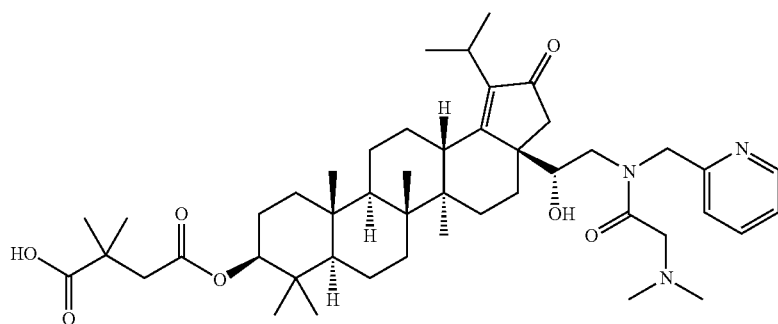
289

290

Example 167

Compound 236

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(2-(dimethylamino)-N-(pyridin-2-ylmethyl)
 acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid 10



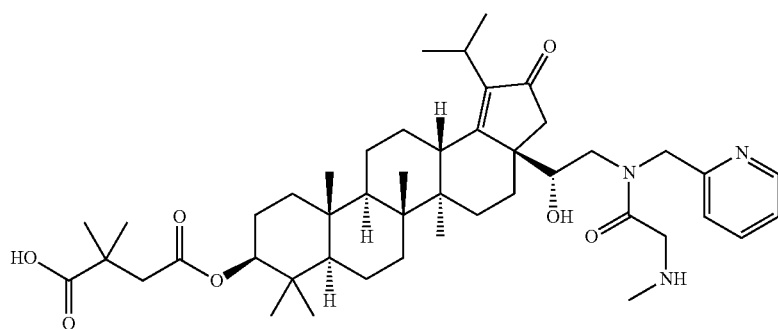
236

LC/MS: m/z calculated 789.5. found 790.5 (M+1)⁺ 35

Example 168

Compound 237

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-(2-(methylamino)-N-(pyridin-2-
 ylmethyl)acetamido)ethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid 45



237

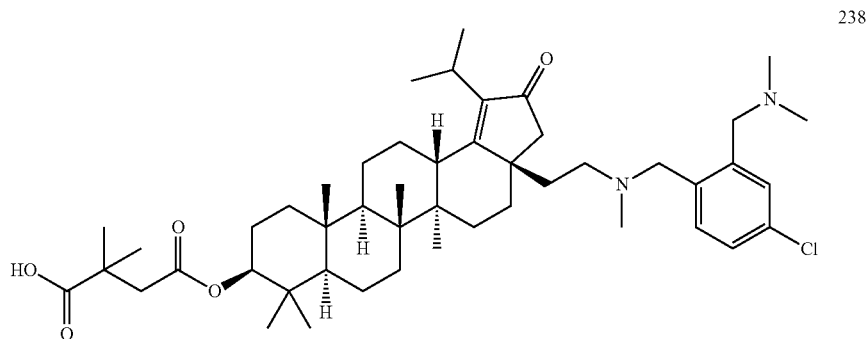
LC/MS: m/z calculated 775.5. found 776.5 (M+1)⁺

Example 169

Compound 238

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((4-chloro-2-((dimethylamino)methyl)benzyl)(me-
 thyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



238

LC/MS: m/z calculated 792.5. found 793.5 (M+1)⁺

Example 170

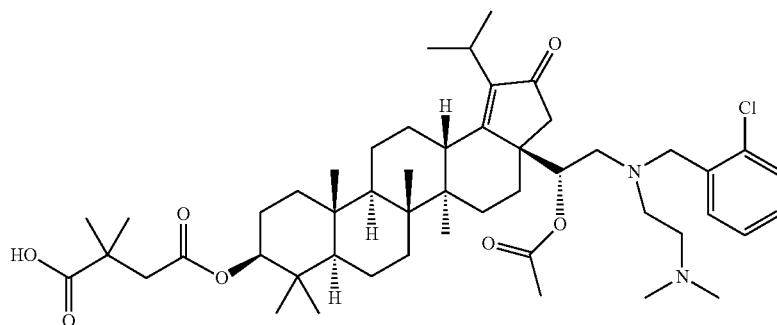
35

Compound 239

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-acetoxy-2-((2-chlorobenzyl)(2-(dimethy-
 lamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid

40

45



239

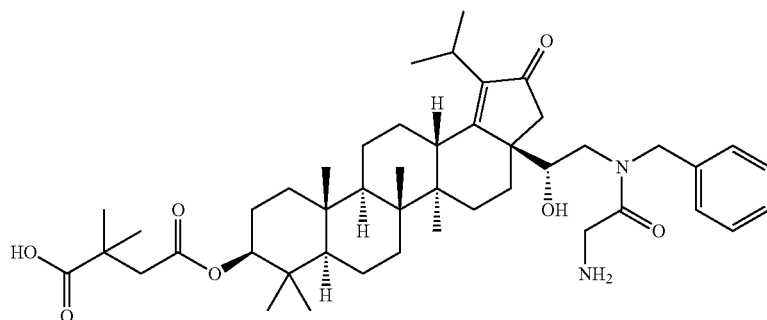
LC/MS: m/z calculated 850.5. found 851.5 (M+1)⁺

Example 171

Compound 240

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-amino-N-benzylacetamido)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



240

LC/MS: m/z calculated 760.5. found 761.5 (M+1)⁺

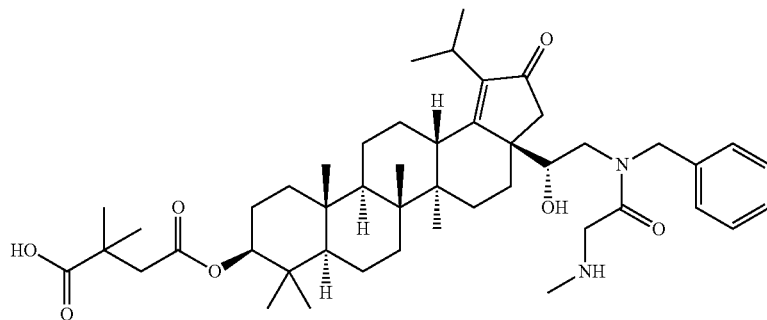
35

Example 172

Compound 241

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-benzyl-2-(methylamino)acetamido)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



241

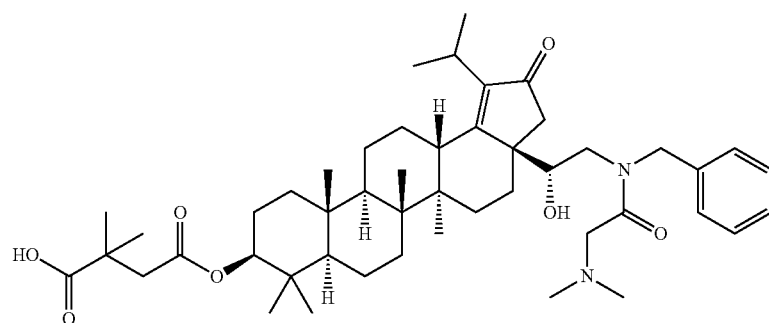
LC/MS: m/z calculated 774.5. found 775.5 (M+1)⁺

Example 173

Compound 242

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-benzyl-2-(dimethylamino)acetamido)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



242

LC/MS: m/z calculated 788.5. found 789.5 (M+1)⁺

35

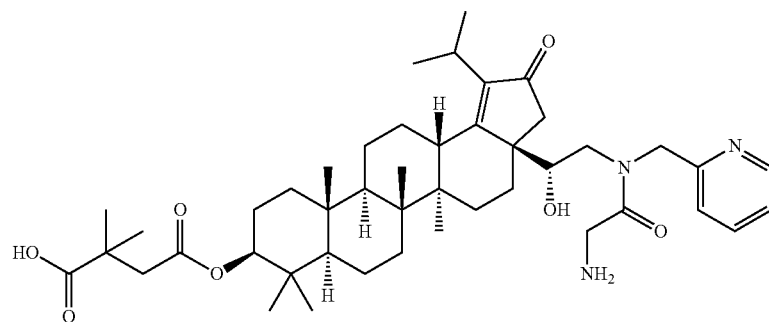
Example 174

Compound 243

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-amino-N-(pyridin-2-ylmethyl)acetamido)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



243

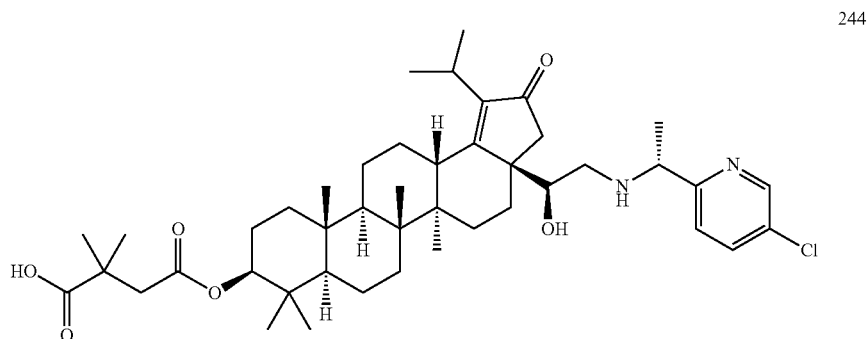
LC/MS: m/z calculated 761.5. found 762.5 (M+1)⁺

Example 175

Compound 244

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(((R)-1-(5-chloropyridin-2-yl)ethyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

5



244

LC/MS: m/z calculated 752.5. found 753.5 (M+1)⁺

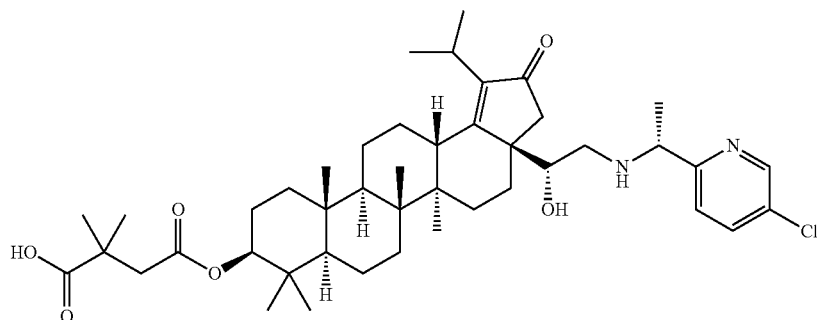
35

Example 176

Compound 245

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((R)-1-(5-chloropyridin-2-yl)ethyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



245

LC/MS: m/z calculated 752.5. found 753.4 (M+1)⁺

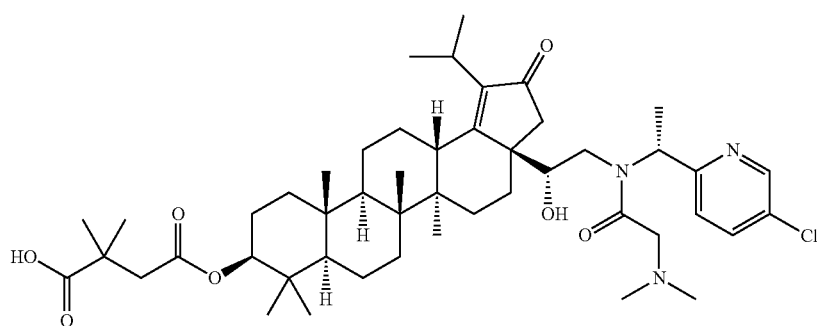
Example 177

Compound 246

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(N—((R)-1-(5-chloropyridin-2-yl)ethyl)-2-
 (dimethylamino)acetamido)-1-hydroxyethyl)-1-iso-
 propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
 5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5

10



246

LC/MS: m/z calculated 837.5. found 838.5 (M+1)⁺

35

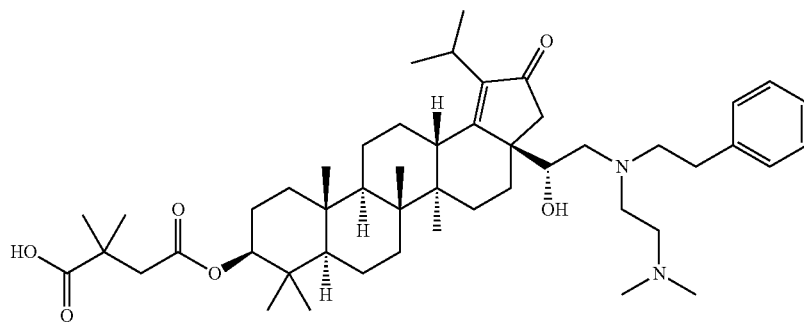
Example 178

Compound 247

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
 2-((2-(dimethylamino)ethyl)(phenethyl)amino)-1-
 hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



247

LC/MS: m/z calculated 788.6. found 789.5 (M+1)⁺

301

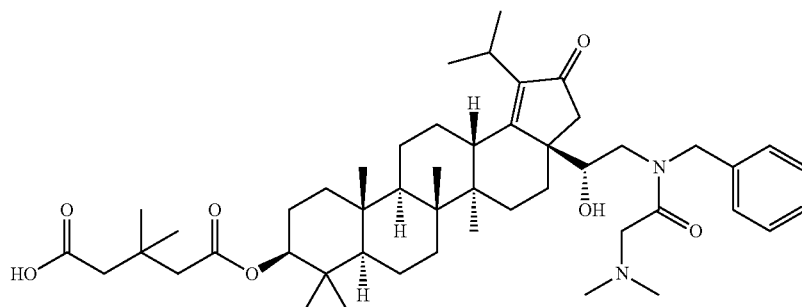
Example 179

302

Compound 248

5-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(N-benzyl-2-(dimethylamino)acetamido)-1-
 hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-3,3-dimethyl-5-oxopentanoic acid

5



248

LC/MS: m/z calculated 802.6. found 803.5 (M+1)⁺

35

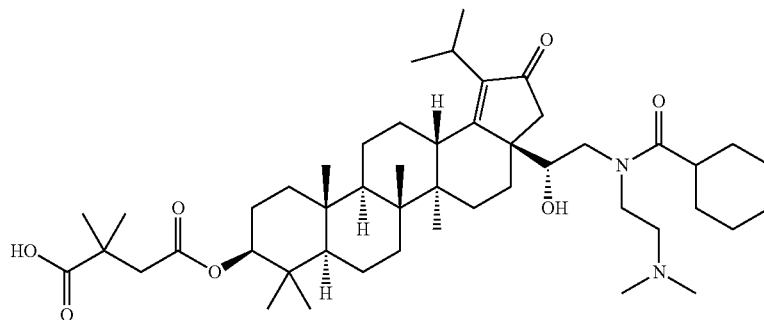
Example 180

Compound 249

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(N-(2-(dimethylamino)ethyl)cyclohexanecar-
 boxamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid

40

45



249

LC/MS: m/z calculated 794.6. found 795.5 (M+1)⁺

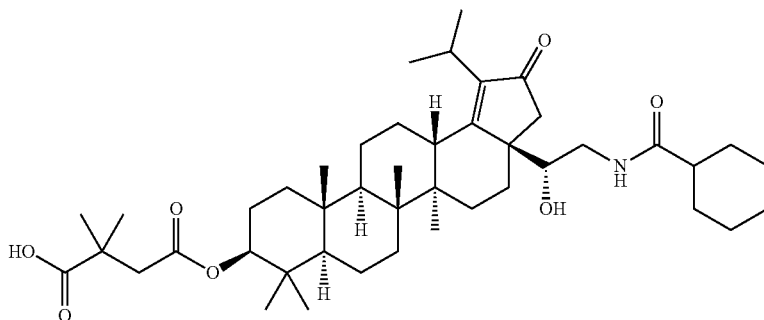
Example 181

Compound 250

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(cyclohexanecarboxamido)-1-hydroxyethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5

250



LC/MS: m/z calculated 723.5. found 724.5 (M+1)⁺

35

Example 182

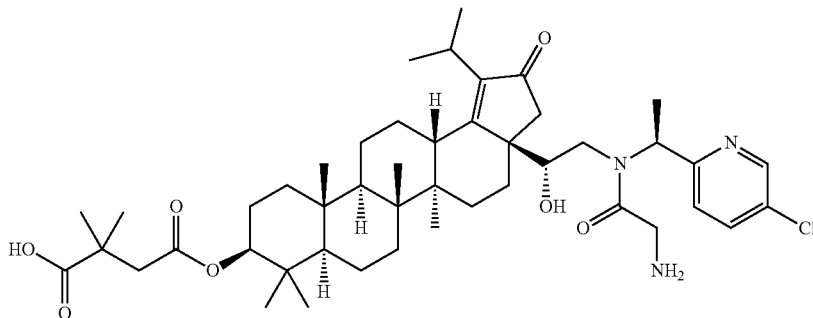
Compound 251

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-amino-N—((S)-1-(5-chloropyridin-2-yl)
ethyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

45

251



LC/MS: m/z calculated 809.5. found 810.4 (M+1)⁺

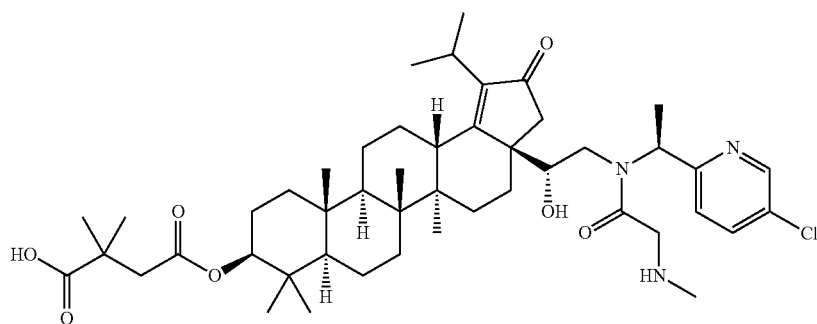
Example 183

Compound 252

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(N—((S)-1-(5-chloropyridin-2-yl)ethyl)-2-
 (methylamino)acetamido)-1-hydroxyethyl)-1-isopro-
 pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
 6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
 2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid

5

10



252

35

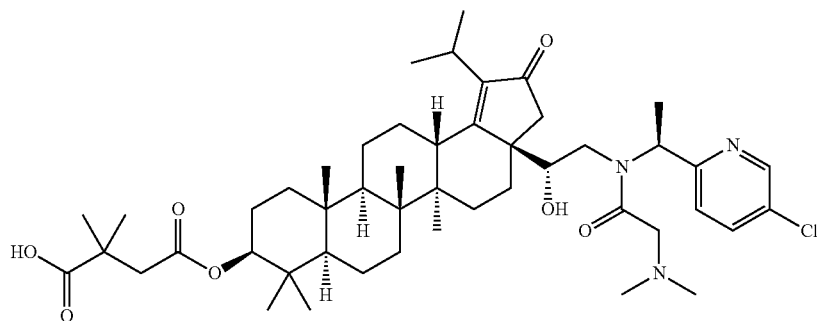
LC/MS: m/z calculated 823.5. found 824.5 (M+1)⁺

Example 184

Compound 253

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(N—((S)-1-(5-chloropyridin-2-yl)ethyl)-2-
 (dimethylamino)acetamido)-1-hydroxyethyl)-1-iso-
 propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
 5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

45



253

LC/MS: m/z calculated 837.5. found 838.5 (M+1)⁺

307

308

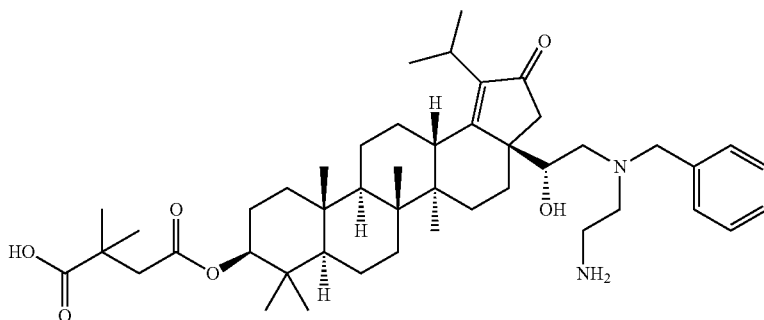
Example 185

Compound 254

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((2-aminoethyl)(benzyl)amino)-1-hydroxy-
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5

254



LC/MS: m/z calculated 746.5. found 747.5 (M+1)⁺

Example 186

35

Compound 255

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((cyclobutylmethyl)amino)-1-hydroxyethyl)-
 1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
 5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40

45

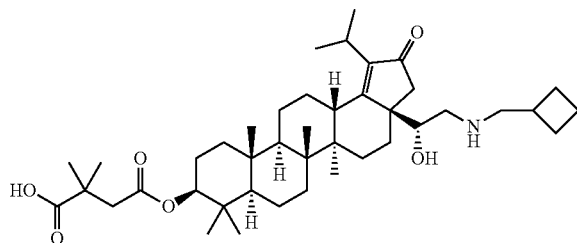
50

255

55

60

65



LC/MS: m/z calculated 681.5. found 682.5 (M+1)⁺

309

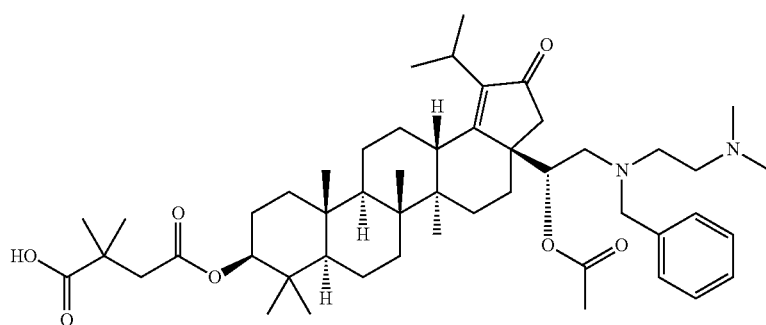
310

Example 187

Compound 256

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-acetoxy-2-(benzyl(2-(dimethylamino)ethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



256

LC/MS: m/z calculated 816.6. found 817.5 (M+1)⁺

35

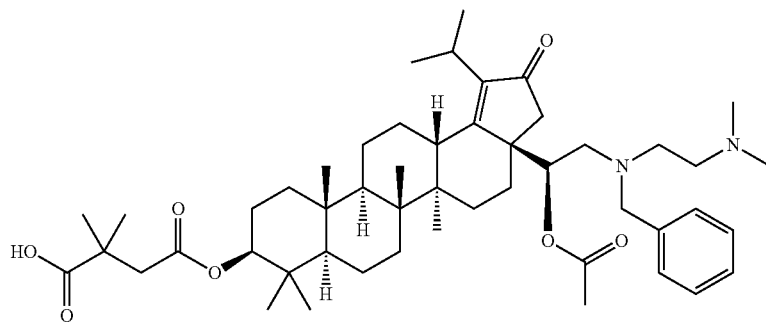
Example 188

Compound 257

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-acetoxy-2-(benzyl(2-(dimethylamino)ethyl)amino)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



257

LC/MS: m/z calculated 816.6. found 817.5 (M+1)⁺

311

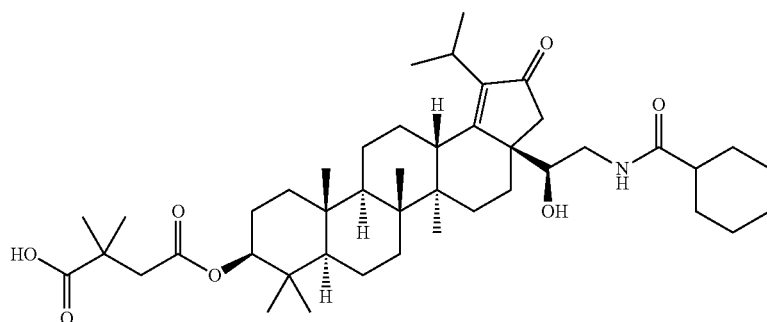
312

Example 189

Compound 258

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(cyclohexanecarboxamido)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



258

LC/MS: m/z calculated 723.5. found 724.5 (M+1)⁺

35

Example 190

Compound 259

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((cyclobutylmethyl)amino)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45

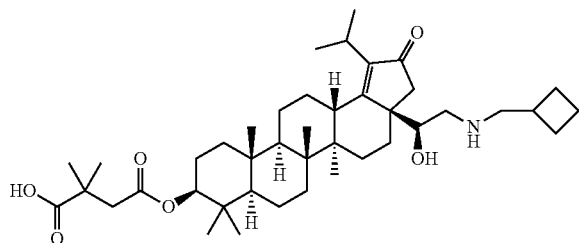
50

259

55

60

65



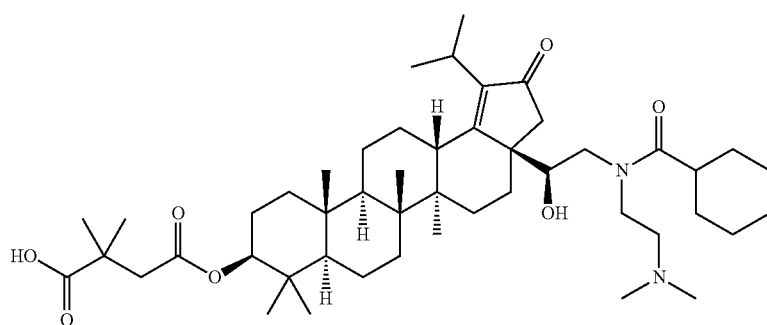
LC/MS: m/z calculated 681.5. found 682.5 (M+1)⁺

Example 191

Compound 260

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(N-(2-(dimethylamino)ethyl)cyclohexanecarboxa-
mido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



260

LC/MS: m/z calculated 794.6. found 795.6 (M+1)⁺

35

Example 192

Compound 261

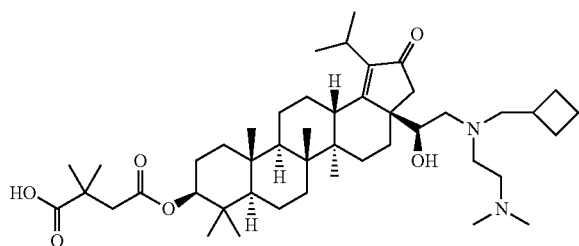
40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((cyclobutylmethyl)(2-(dimethylamino)ethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

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261



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65

LC/MS: m/z calculated 752.6. found 753.6 (M+1)⁺

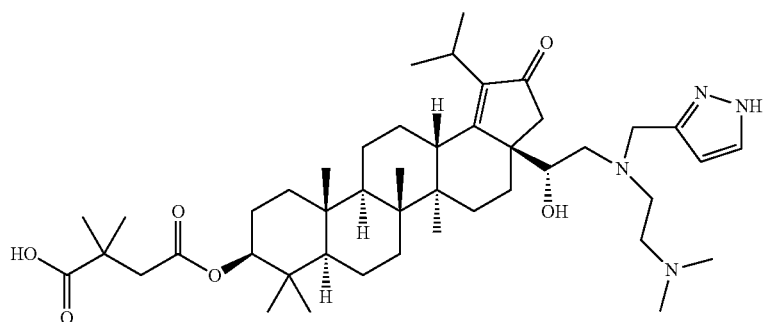
315

Example 193

316

Compound 262

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((1H-pyrazol-3-yl)methyl)(2-(dimethyl-
amino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 5 10



262

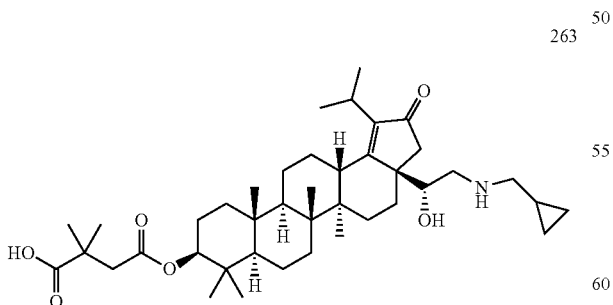
LC/MS: m/z calculated 764.6. found 765.5 (M+1)⁺

35

Example 194

Compound 263

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((cyclopropylmethyl)amino)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid 45



263

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LC/MS: m/z calculated 667.5. found 668.5 (M+1)⁺

317

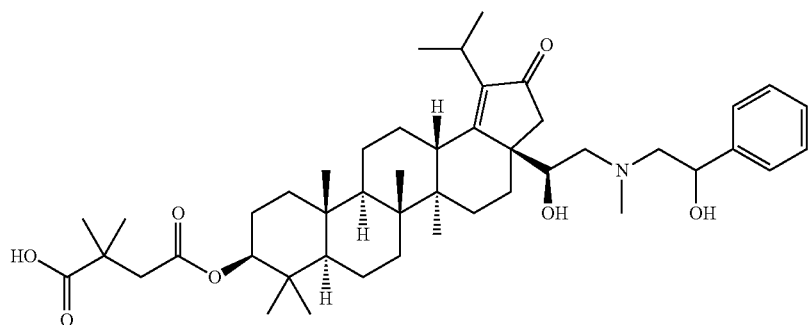
318

Example 195

Compound 264

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((1S)-1-hydroxy-2-((2-hydroxy-2-phenylethyl)(me-
thyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



264

LC/MS: m/z calculated 747.5. found 748.5 (M+1)⁺

35

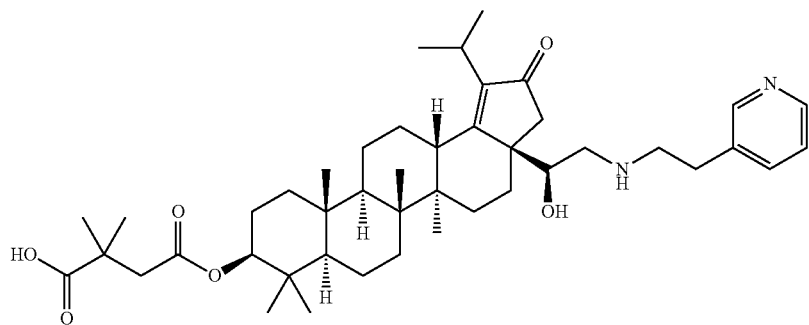
Example 196

Compound 265

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-((2-(pyridin-3-yl)ethyl)amino)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



265

LC/MS: m/z calculated 718.5. found 719.5 (M+1)⁺

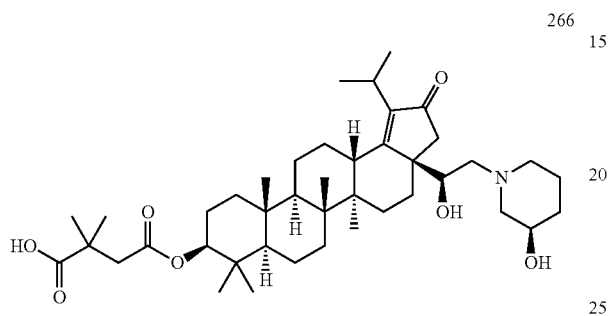
319

320

Example 197

Compound 266

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-((R)-3-hydroxypiperidin-1-yl)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

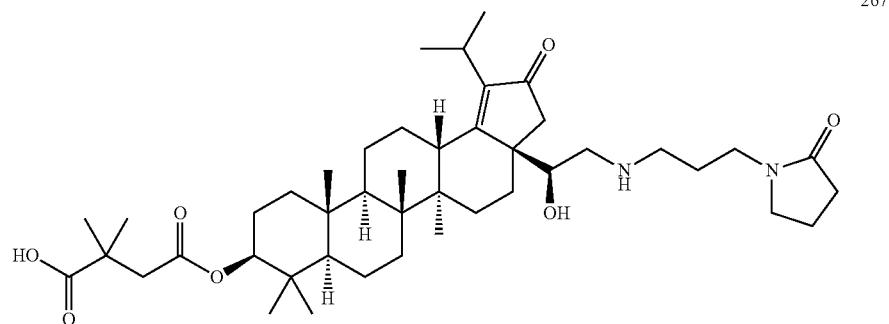


LC/MS: m/z calculated 697.5. found 698.5 (M+1)⁺

Example 198

Compound 267

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-((3-(2-oxopyrrolidin-1-yl)propyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 738.5. found 739.5 (M+1)⁺

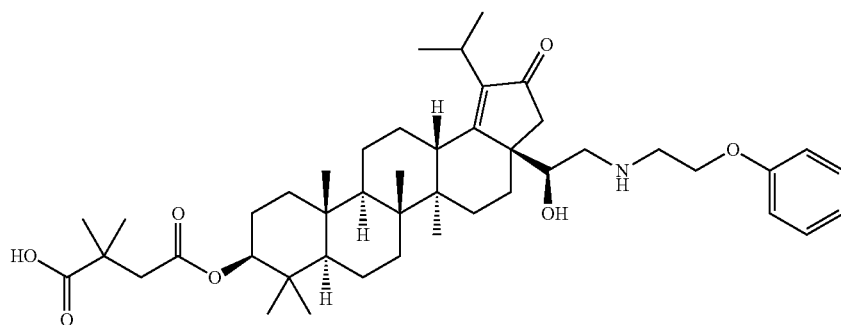
321

Example 199

Compound 268

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-hydroxy-2-((2-phenoxyethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



268

LC/MS: m/z calculated 733.5. found 734.5 (M+1)⁺

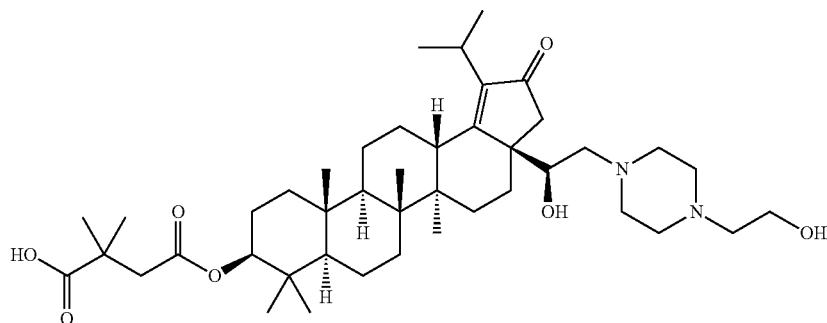
Example 200

25

Compound 269

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-hydroxy-2-(4-(2-hydroxyethyl)piperazin-1-yl)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

30



269

LC/MS: m/z calculated 726.5. found 727.5 (M+1)⁺

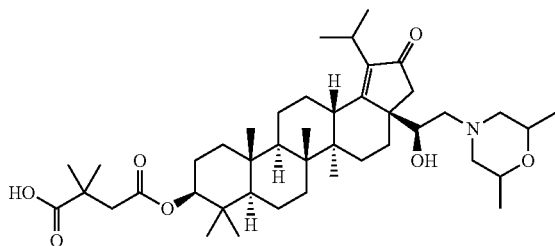
Example 201

Compound 270

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((1S)-2-(2,6-dimethylmorpholino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

50

270



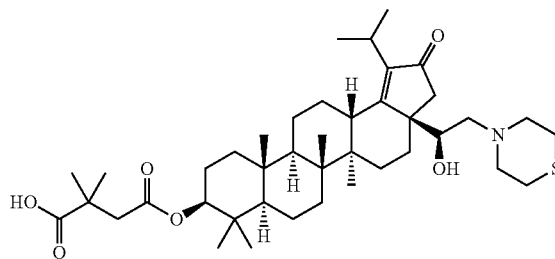
LC/MS: m/z calculated 711.5. found 712.5 (M+1)⁺

Example 202

Compound 271

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-hydroxy-2-thiomorpholinoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

271



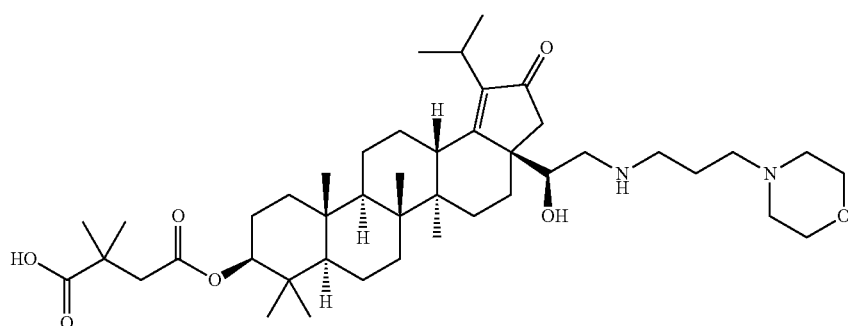
LC/MS: m/z calculated 699.5. found 700.4 (M+1)⁺

Example 203

Compound 272

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-((3-morpholinopropyl)amino)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



272

LC/MS: m/z calculated 740.5. found 741.5 (M+1)⁺

35

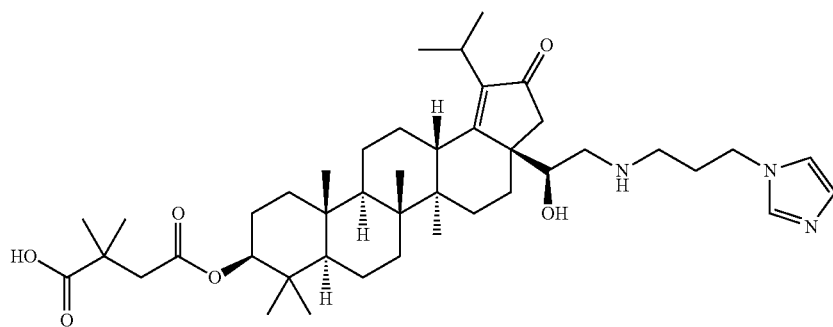
Example 204

Compound 273

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((3-(1H-imidazol-1-yl)propyl)amino)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



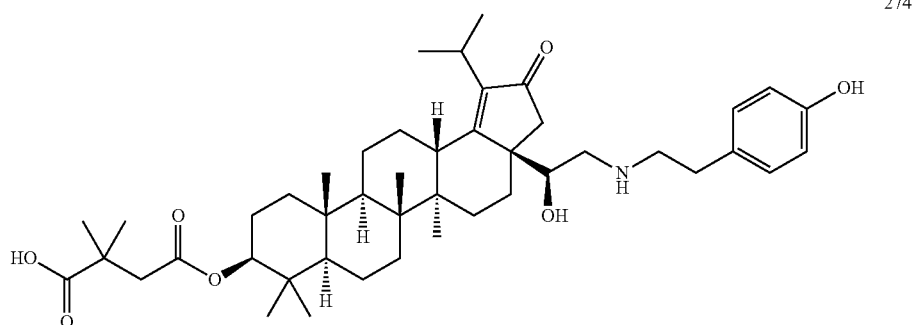
273

LC/MS: m/z calculated 721.5. found 722.5 (M+1)⁺

Example 205

Compound 274

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-((4-hydroxyphenethyl)amino)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

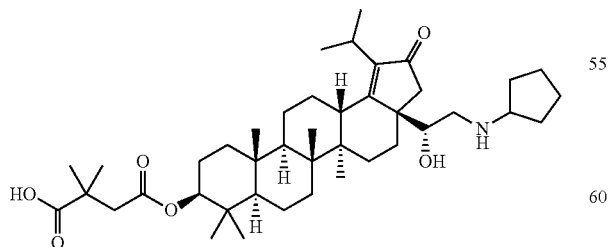


LC/MS: m/z calculated 733.5. found 734.5 (M+1)⁺

Example 206

Compound 275

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(cyclopentylamino)-1-hydroxyethyl)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 681.5. found 682.5 (M+1)⁺

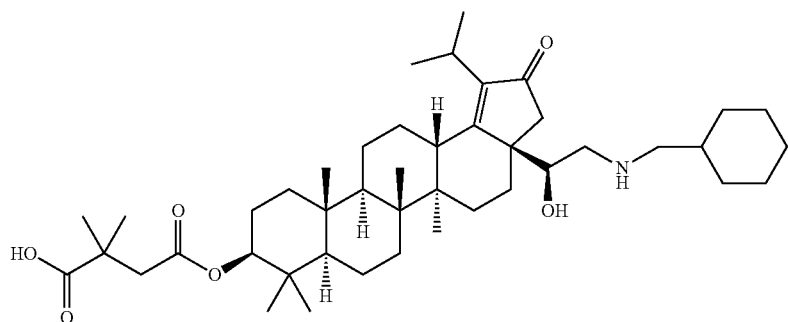
327

328

Example 207

Compound 276

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((cyclohexylmethyl)amino)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



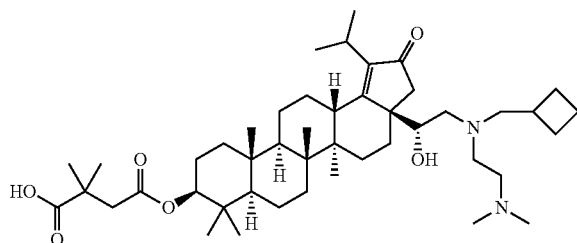
276

LC/MS: m/z calculated 709.5. found 710.5 (M+1)⁺

Example 208

Compound 277

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((cyclobutylmethyl)(2-(dimethylamino)ethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



277

LC/MS: m/z calculated 752.6. found 753.6 (M+1)⁺

329

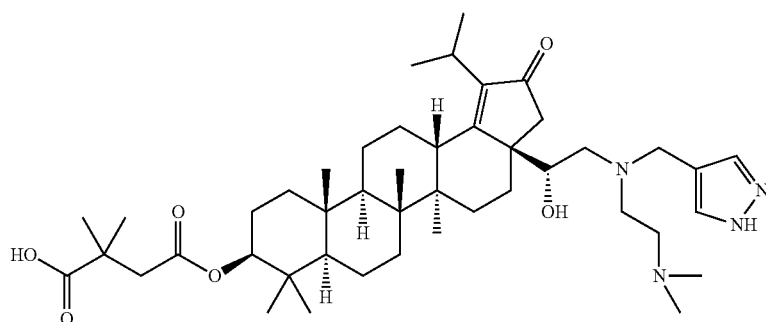
Example 209

Compound 278

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((1H-pyrazol-4-yl)methyl)(2-(dimethyl-
lamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

10



278

LC/MS: m/z calculated 764.6. found 765.5 (M+1)⁺

Example 211

Example 210

35

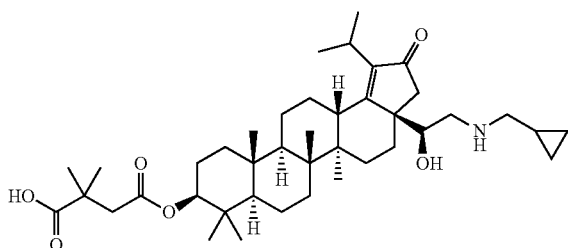
Compound 279

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((cyclopropylmethyl)amino)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45

279 50



55

60

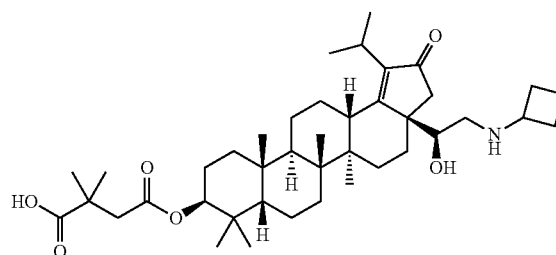
65

LC/MS: m/z calculated 667.5. found 668.5 (M+1)⁺

Compound 280

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(cyclobutylamino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

280



60

LC/MS: m/z calculated 667.5. found 668.5 (M+1)⁺

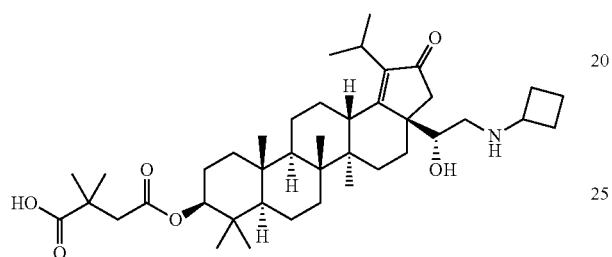
331

332

Example 212

Compound 281

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(cyclobutylamino)-1-hydroxyethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

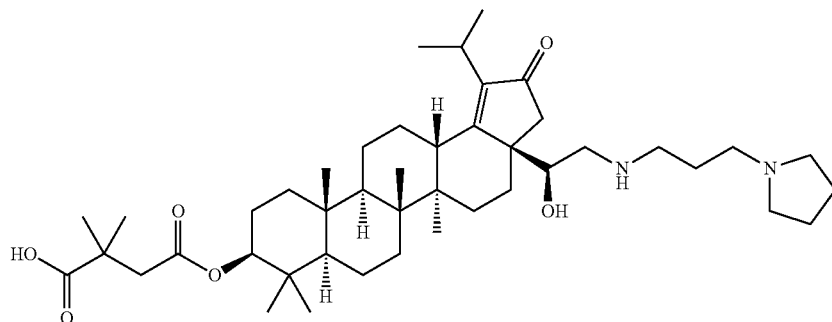


LC/MS: m/z calculated 667.5. found 668.5 (M+1)⁺

Example 213

Compound 282

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-((3-(pyrrolidin-1-yl)propyl)amino)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 724.5. found 725.5 (M+1)⁺

333

Example 214

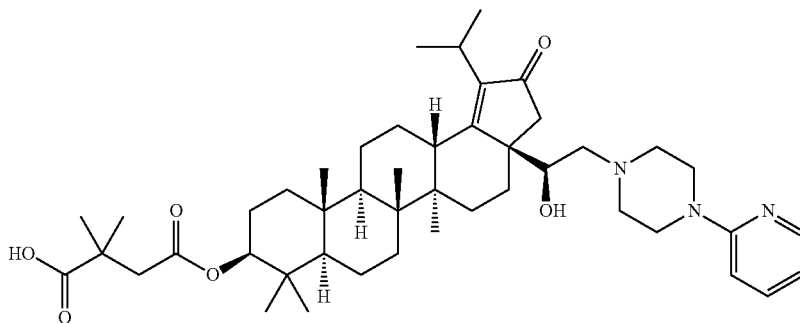
334

Compound 283

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(4-(pyridin-2-yl)piperazin-1-yl)ethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5

283



LC/MS: m/z calculated 759.5. found 760.5 (M+1)⁺

35

Example 215

Compound 284

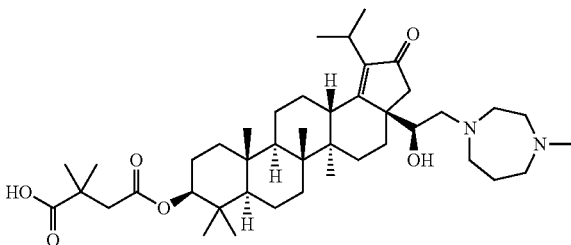
40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(4-methyl-1,4-diazepan-1-yl)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

45

50

284



55

60

65

LC/MS: m/z calculated 710.5. found 711.5 (M+1)⁺

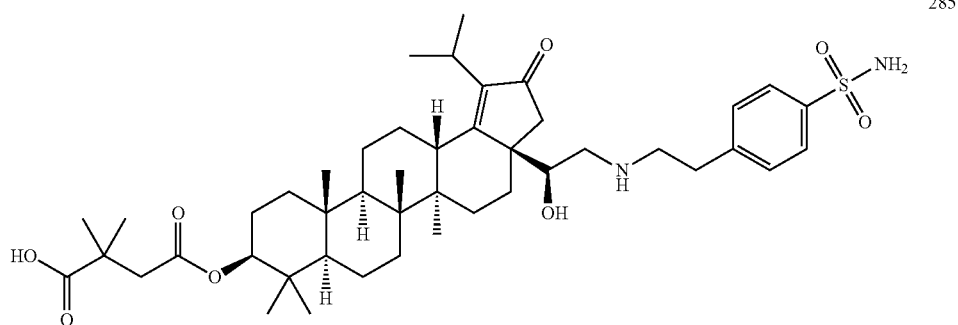
335

Example 216

336

Compound 285

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-((4-sulfamoylphenethyl)amino)ethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



285

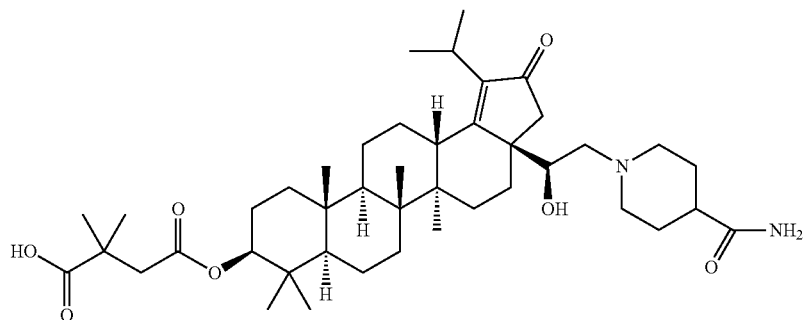
LC/MS: m/z calculated 796.5. found 797.5 (M+1)⁺

35

Example 217

Compound 286

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(4-carbamoylpiperidin-1-yl)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



286

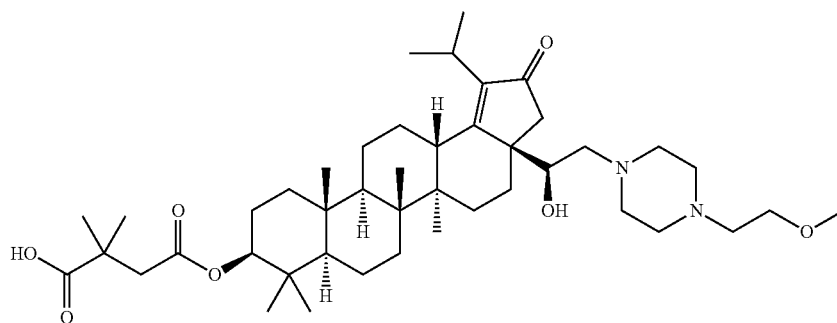
LC/MS: m/z calculated 724.5. found 725.5 (M+1)⁺

Example 218

Compound 287

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(4-(2-methoxyethyl)piperazin-1-yl)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



287

LC/MS: m/z calculated 740.5. found 741.5 (M+1)⁺

35

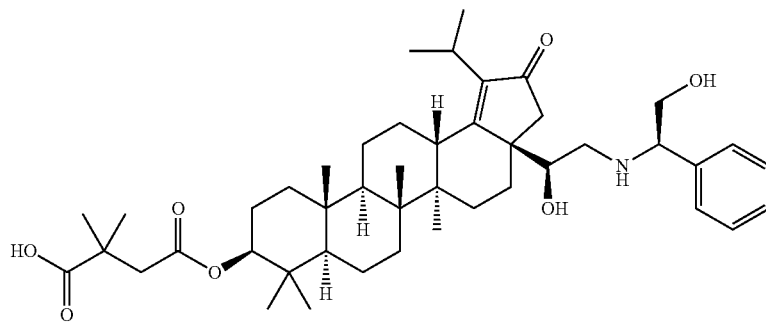
Example 219

Compound 288

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(((R)-2-hydroxy-1-phenylethyl)amino)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



288

LC/MS: m/z calculated 733.5. found 734.5 (M+1)⁺

339

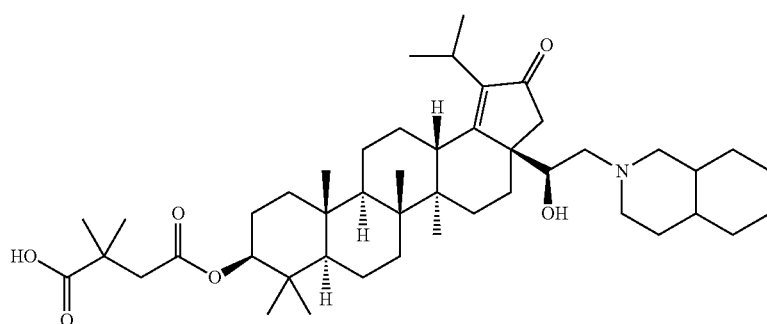
340

Example 220

Compound 289

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((1S)-1-hydroxy-2-(octahydroisoquinolin-2(1H)-yl)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



289

LC/MS: m/z calculated 735.5. found 736.5 (M+1)⁺

35

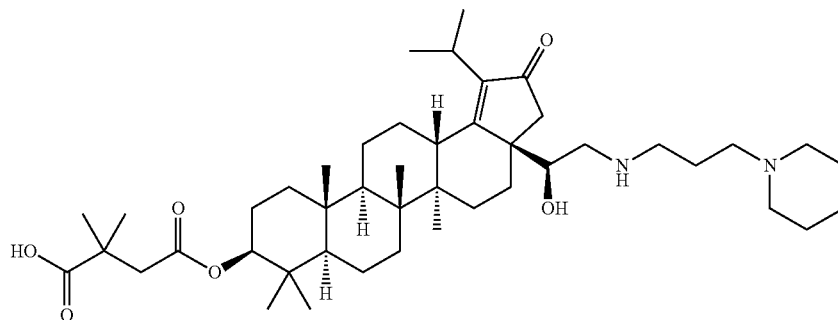
Example 221

Compound 290

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
 1-hydroxy-2-((3-(piperidin-1-yl)propyl)amino)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40

45



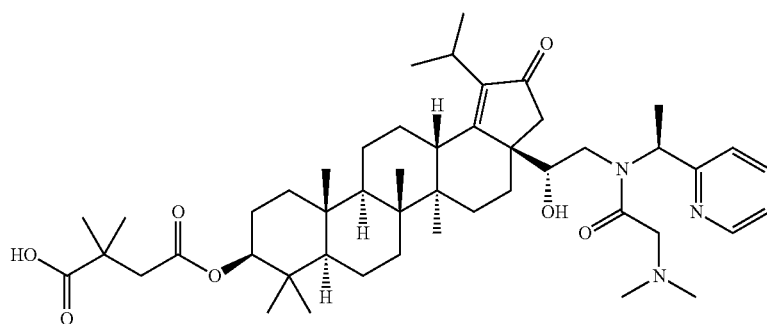
290

LC/MS: m/z calculated 738.5. found 739.5 (M+1)⁺

Example 222

Compound 291

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(2-(dimethylamino)-N-((S)-1-(pyridin-2-yl)
 ethyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,
 8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
 10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid 10



291

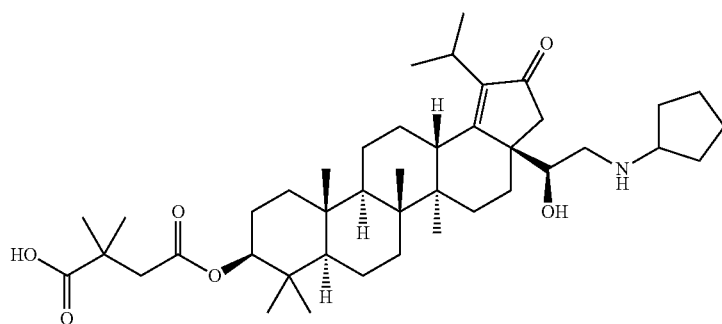
35

LC/MS: m/z calculated 803.5. found 804.5 (M+1)⁺

Example 223

Compound 292

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
 2-(cyclopentylamino)-1-hydroxyethyl)-1-isopropyl-
 5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
 7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid 45



292

LC/MS: m/z calculated 681.5. found 682.5 (M+1)⁺

343

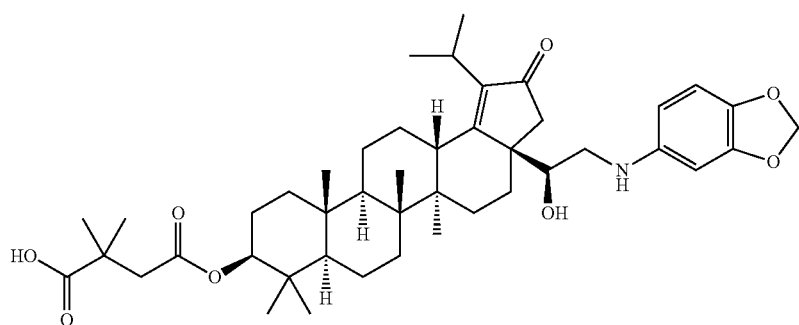
Example 224

344

Compound 293

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(benzo[d][1,3]dioxol-5-ylamino)-1-hydroxyethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



293

LC/MS: m/z calculated 733.5. found 734.5 (M+1)⁺

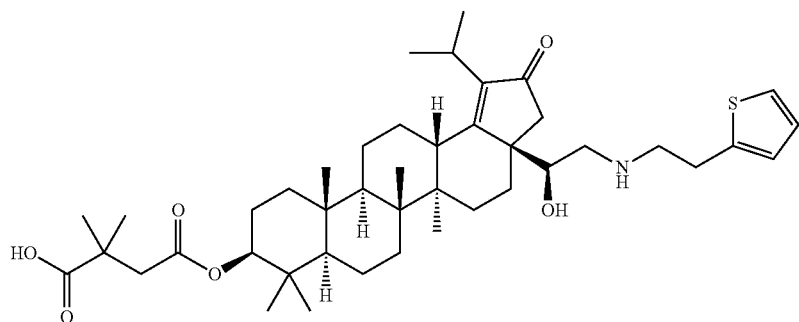
Example 225

35

Compound 294

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-((2-(thiophen-2-yl)ethyl)amino)ethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40



294

LC/MS: m/z calculated 723.5. found 724.4 (M+1)⁺

345

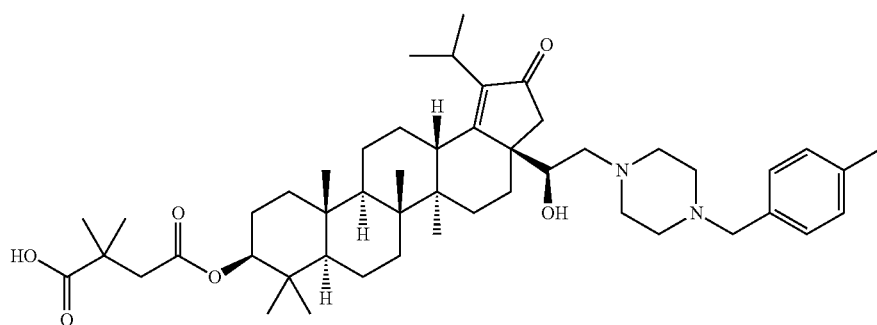
Example 226

346

Compound 295

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(4-(4-methylbenzyl)piperazin-1-yl)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



295

LC/MS: m/z calculated 786.5. found 787.5 (M+1)⁺

35

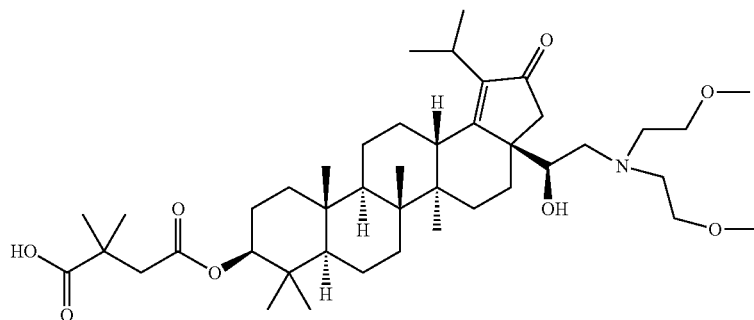
Example 227

Compound 296

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(bis(2-methoxyethyl)amino)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



296

LC/MS: m/z calculated 729.5. found 730.5 (M+1)⁺

347

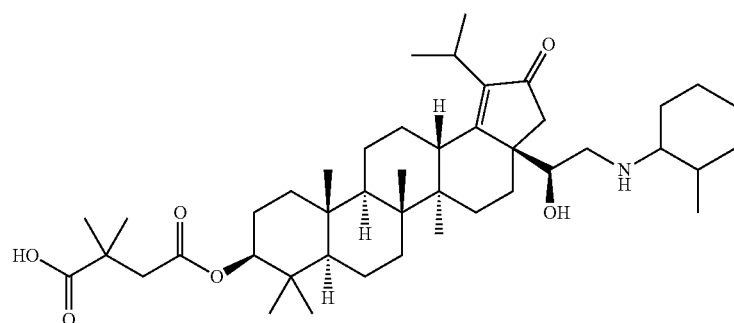
Example 228

348

Compound 297

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((1S)-1-hydroxy-2-((2-methylcyclohexyl)amino)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



297

LC/MS: m/z calculated 709.5. found 710.5 (M+1)⁺

35

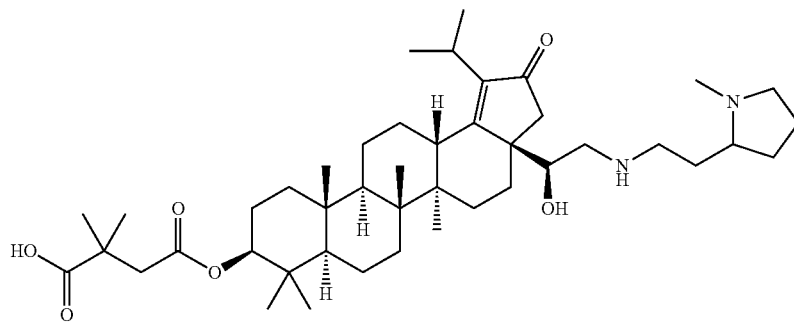
Example 229

Compound 298

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((1S)-1-hydroxy-2-((2-(1-methylpyrrolidin-2-yl)
 ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pen-
 tamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,
 11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
 chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



298

LC/MS: m/z calculated 724.5. found 725.5 (M+1)⁺

349

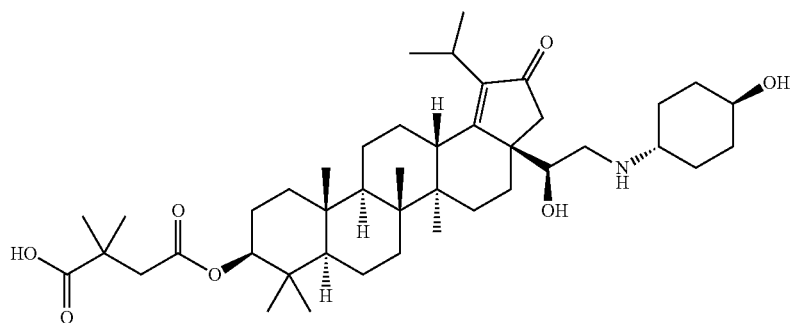
350

Example 230

Compound 299

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(((1r,4S)-4-hydroxycyclohexyl)amino)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



299

LC/MS: m/z calculated 711.5. found 712.4 (M+1)⁺

35

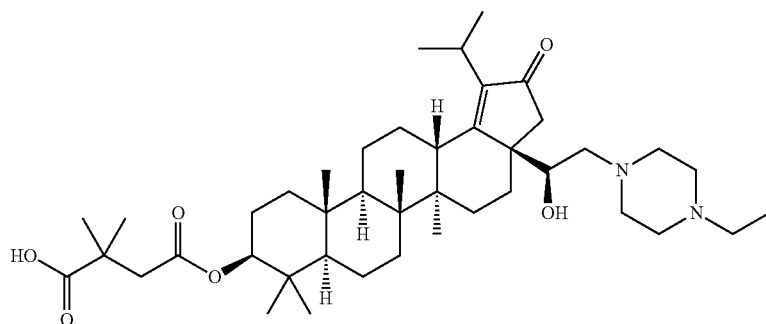
Example 231

Compound 300

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(4-ethylpiperazin-1-yl)-1-hydroxyethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

45



300

LC/MS: m/z calculated 710.5. found 711.5 (M+1)⁺

351

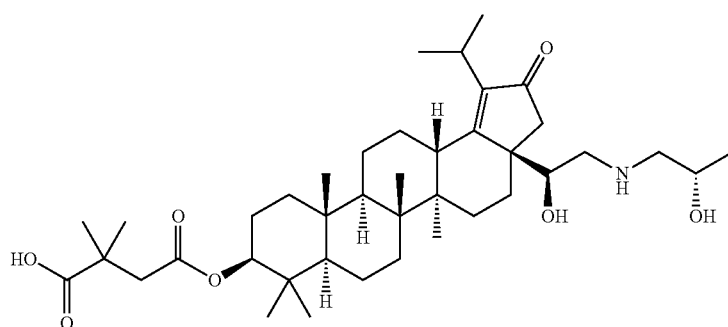
Example 232

352

Compound 301

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(((S)-2-hydroxypropyl)amino)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



301

LC/MS: m/z calculated 671.5. found 672.4 (M+1)⁺

35

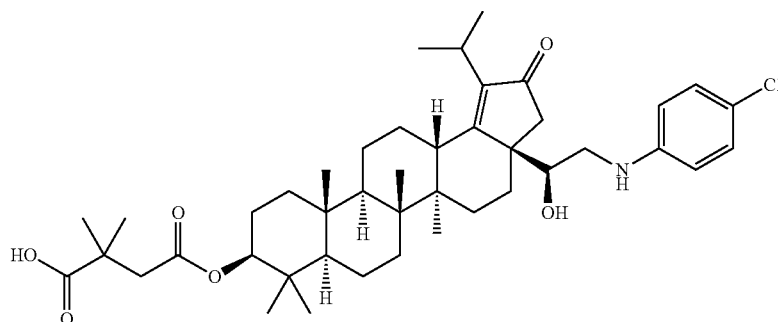
Example 233

Compound 302

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chlorophenyl)amino)-1-hydroxyethyl)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



302

LC/MS: m/z calculated 723.4. found 724.4 (M+1)⁺

353

354

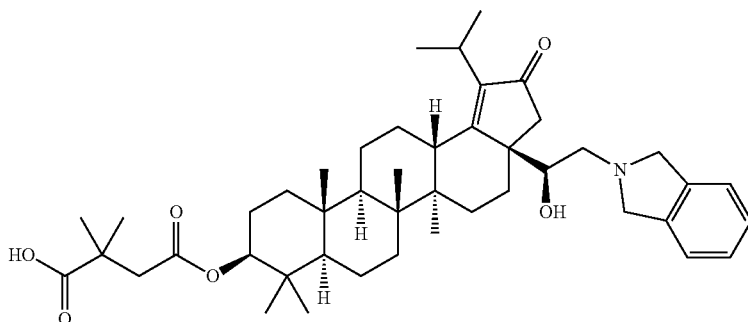
Example 234

Compound 303

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(isoindolin-2-yl)ethyl)-1-isopropyl-5a,
5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

303



LC/MS: m/z calculated 715.5. found 716.5 (M+1)⁺

35

Example 235

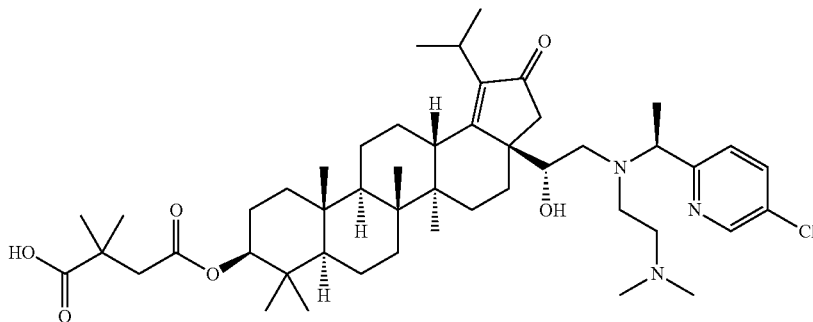
Compound 304

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((S)-1-(5-chloropyridin-2-yl)ethyl)(2-(dim-
ethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

45

304



LC/MS: m/z calculated 823.5. found 824.5 (M+1)⁺

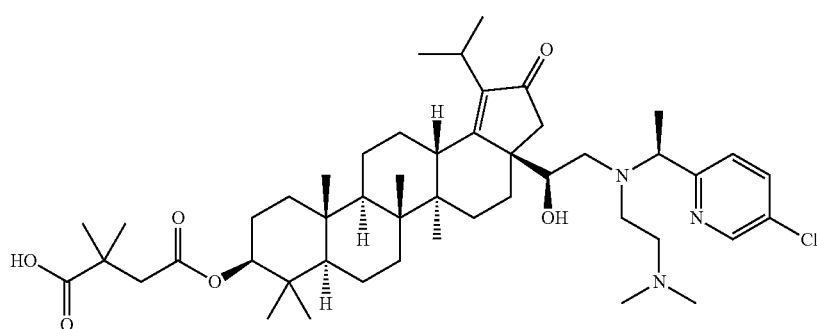
355

Example 236

356

Compound 305

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(((S)-1-(5-chloropyridin-2-yl)ethyl)(2-(dimethyl-
lamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 5 10



305

35

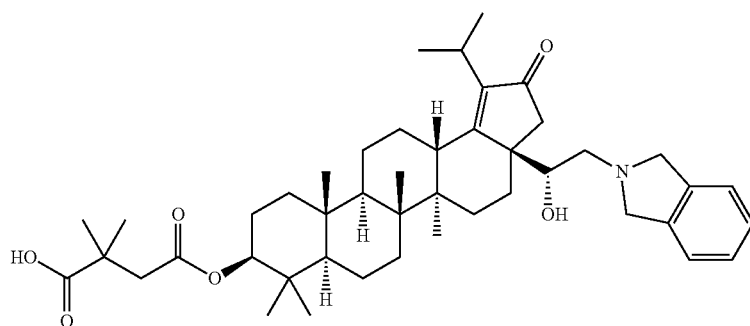
LC/MS: m/z calculated 823.5. found 824.5 (M+1)⁺

Example 237

Compound 306

40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(isoindolin-2-yl)ethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 45



306

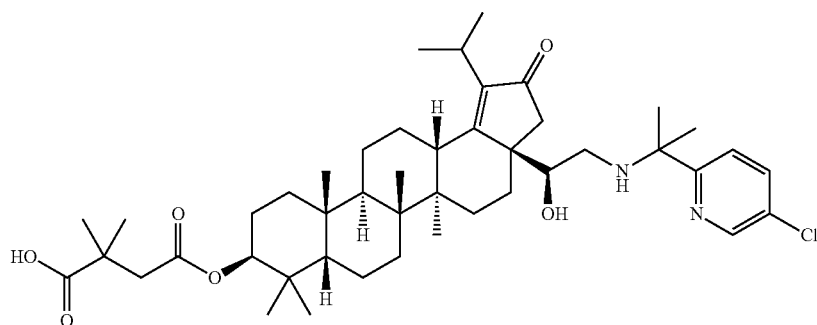
LC/MS: m/z calculated 715.5. found 716.5 (M+1)⁺

Example 238

Compound 307

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((2-(5-chloropyridin-2-yl)propan-2-yl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentameth-
yl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



307

LC/MS: m/z calculated 766.5. found 767.5 (M+1)⁺

35

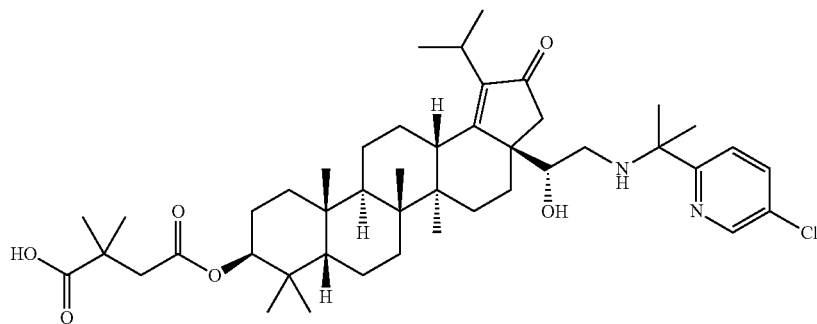
Example 239

Compound 308

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(5-chloropyridin-2-yl)propan-2-yl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



308

LC/MS: m/z calculated 766.5. found 767.6 (M+1)⁺

359

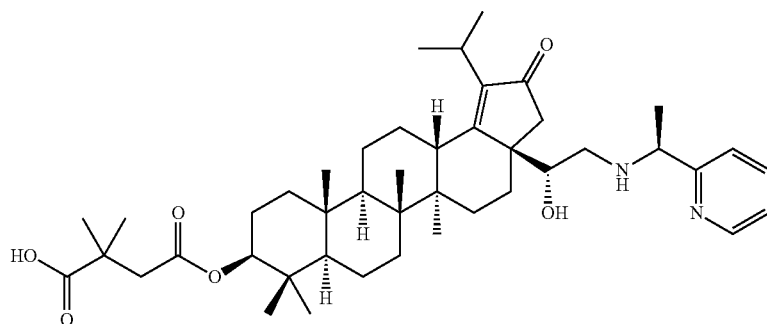
Example 240

360

Compound 309

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-(((S)-1-(pyridin-2-yl)ethyl)amino)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



309

LC/MS: m/z calculated 718.5. found 719.5 (M+1)⁺

35

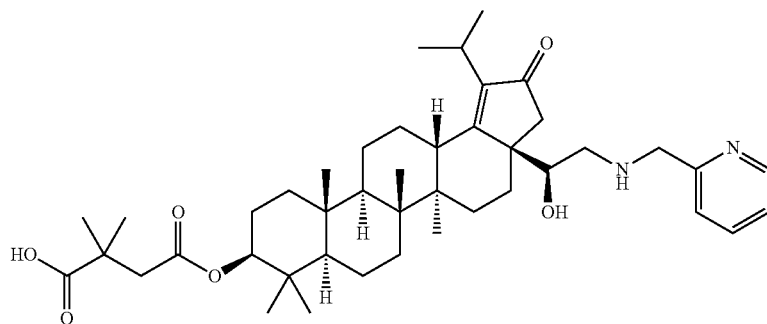
Example 241

Compound 310

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
 1-hydroxy-2-((pyridin-2-ylmethyl)amino)ethyl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40

45



310

LC/MS: m/z calculated 704.5. found 705.5 (M+1)⁺

361

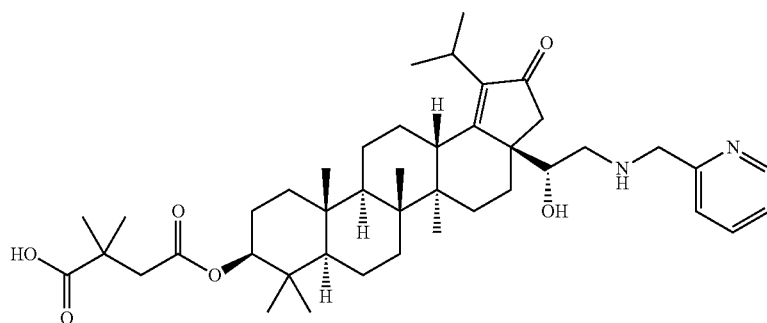
Example 242

362

Compound 311

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((pyridin-2-ylmethyl)amino)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



311

LC/MS: m/z calculated 704.5. found 705.5 (M+1)⁺

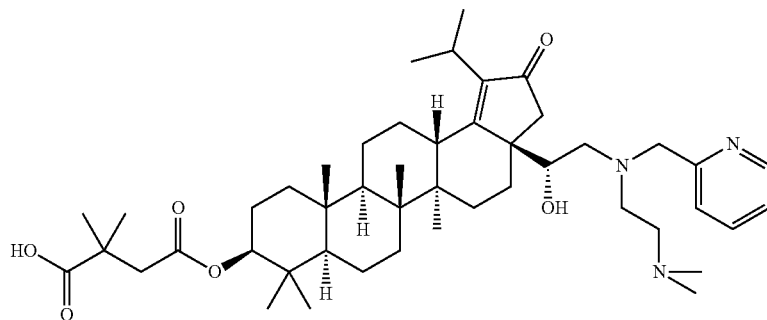
Example 243

35

Compound 312

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(pyridin-2-ylm-
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

40



312

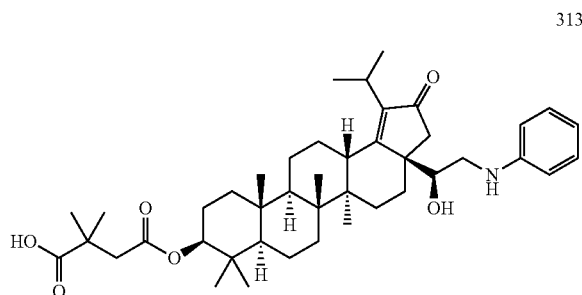
LC/MS: m/z calculated 775.5. found 776.5 (M+1)⁺

363

Example 244

Compound 313

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-hydroxy-2-(phenylamino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

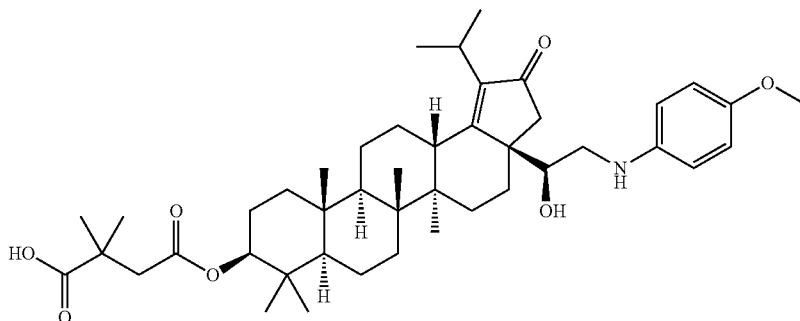


LC/MS: m/z calculated 689.5. found 690.5 (M+1)⁺

Example 245

Compound 314

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-hydroxy-2-((4-methoxyphenyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 719.5. found 720.5 (M+1)⁺

364

Example 246

Compound 315

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-hydroxy-2-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

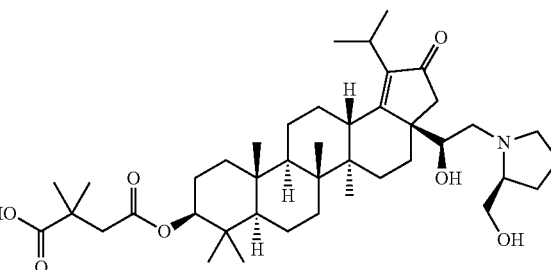
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315

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LC/MS: m/z calculated 697.5. found 698.5 (M+1)⁺

Example 247

Compound 316

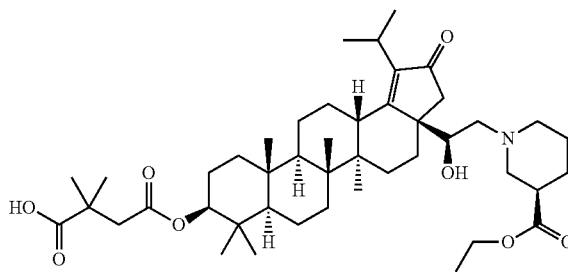
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((R)-3-(ethoxycarbonyl)piperidin-1-yl)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

35

316

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LC/MS: m/z calculated 753.5. found 754.5 (M+1)⁺

314

65

Example 248

Compound 317

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(4-formylpiperazin-1-yl)-1-hydroxyethyl)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5

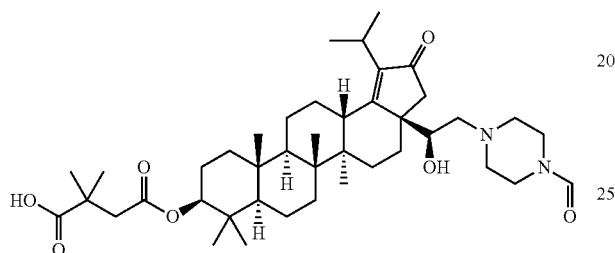
10

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317

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25



LC/MS: m/z calculated 710.5. found 711.5 (M+1)⁺

30

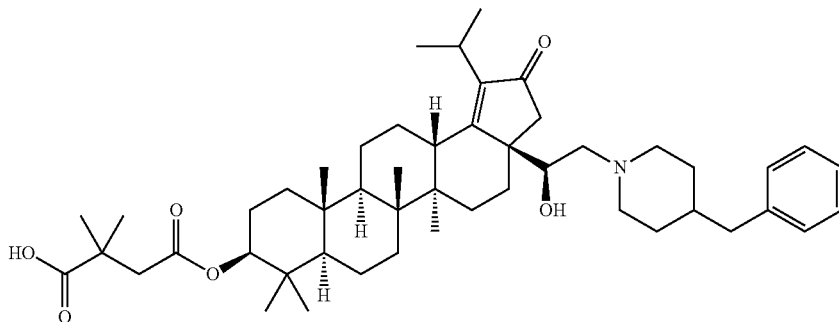
Example 249

Compound 318

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(4-benzylpiperidin-1-yl)-1-hydroxyethyl)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

35

318



LC/MS: m/z calculated 771.5. found 772.5 (M+1)⁺

367

368

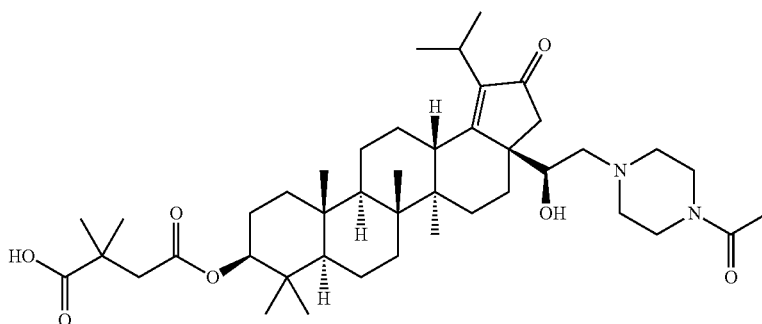
Example 250

Compound 319

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(4-acetylpiperazin-1-yl)-1-hydroxyethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

319



LC/MS: m/z calculated 724.5. found 725.5 (M+1)⁺

35

Example 251

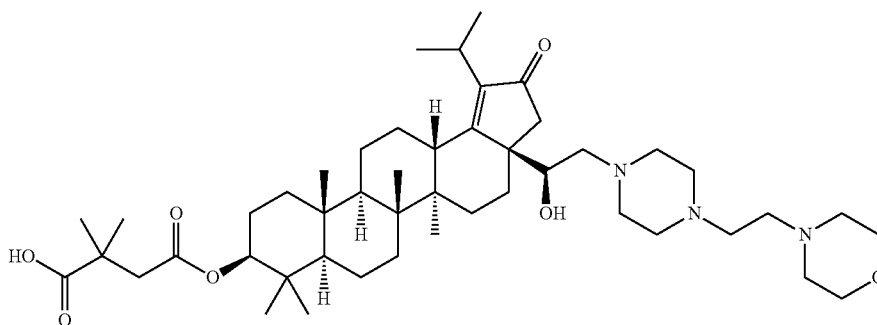
Compound 320

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(4-(2-morpholinoethyl)piperazin-1-yl)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

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320



LC/MS: m/z calculated 795.6. found 796.5 (M+1)⁺

369

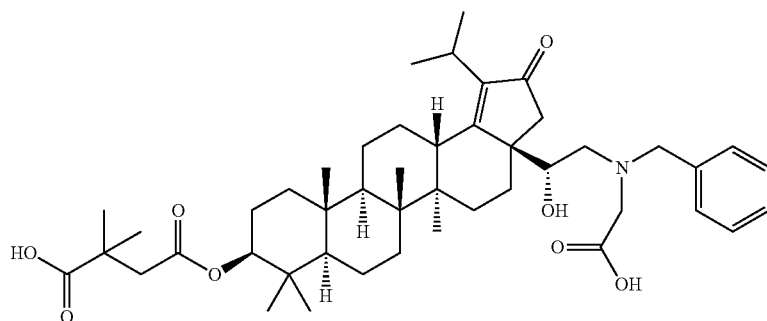
370

Example 252

Compound 321

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(benzyl(carboxymethyl)amino)-1-hydroxy-
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



321

LC/MS: m/z calculated 761.5. found 762.5 (M+1)⁺

35

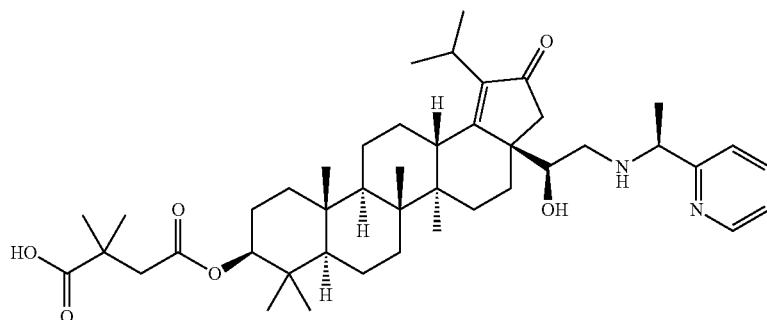
Example 253

Compound 322

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
 1-hydroxy-2-(((S)-1-(pyridin-2-yl)ethyl)amino)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40

45



322

LC/MS: m/z calculated 718.5. found 719.5 (M+1)⁺

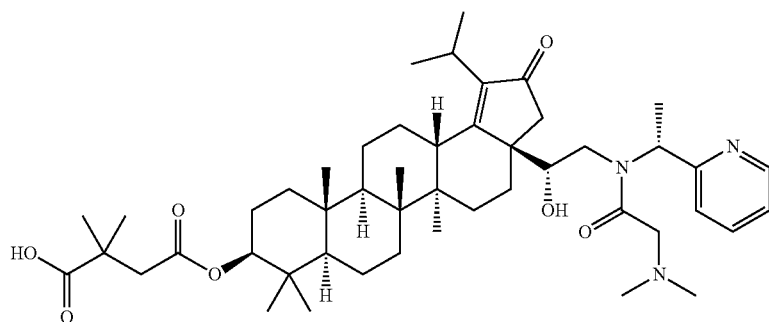
371

Example 254

372

Compound 323

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(2-(dimethylamino)-N-((R)-1-(pyridin-2-yl)
 ethyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,
 8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
 10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid 5 10



323

35

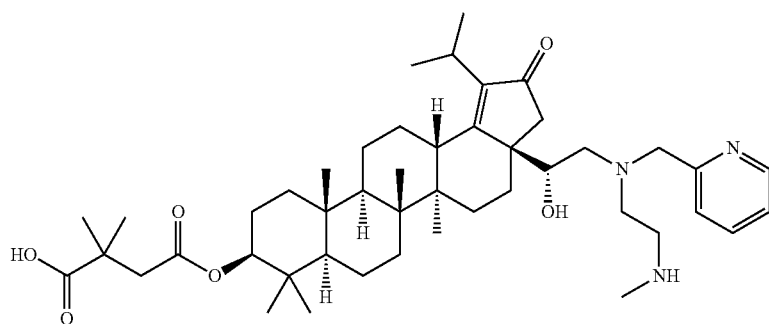
LC/MS: m/z calculated 803.5. found 804.5 (M+1)⁺

Example 255

Compound 324

40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((2-(methylamino)ethyl)(pyridin-
 2-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-
 pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
 11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
 chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid 45



324

LC/MS: m/z calculated 761.5. found 762.5 (M+1)⁺

373

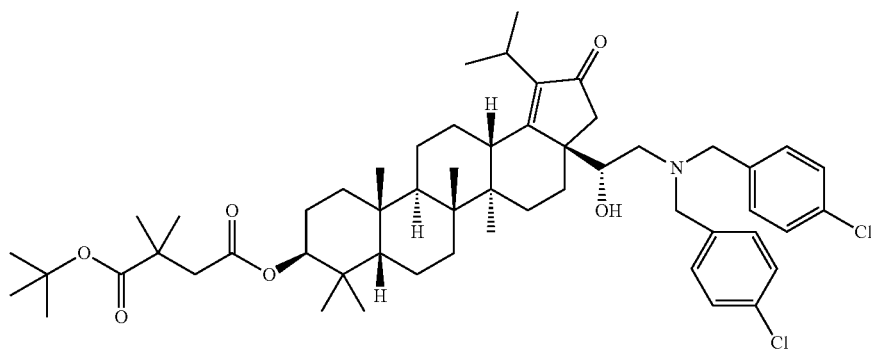
Example 256

374

Compound 325

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-
2-(bis(4-chlorobenzyl)amino)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-
butyl 2,2-dimethylsuccinate

5



325

LC/MS: m/z calculated 917.5. found 918.5 (M+1)⁺

35

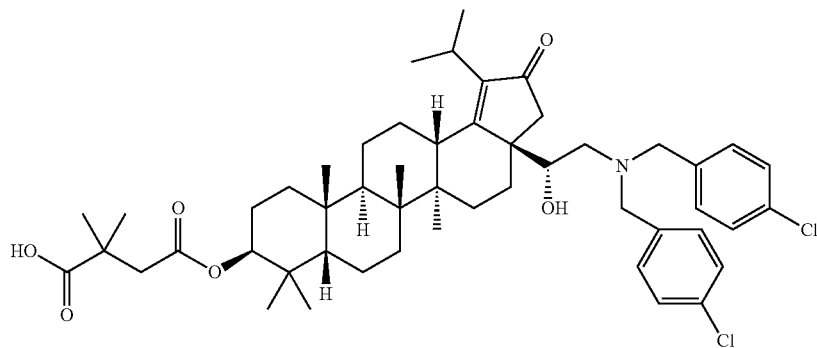
Example 257

Compound 326

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(bis(4-chlorobenzyl)amino)-1-hydroxyethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



326

LC/MS: m/z calculated 861.4. found 862.4 (M+1)⁺

375

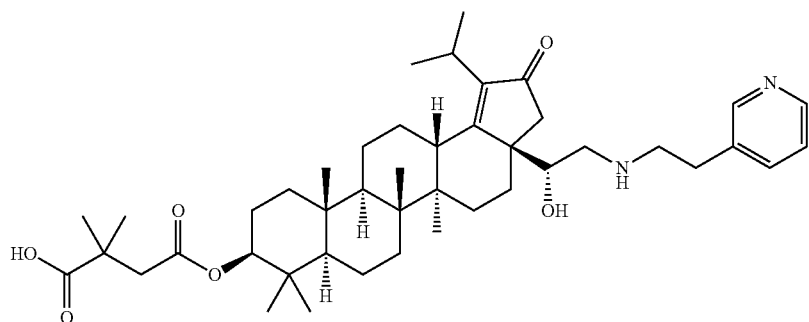
Example 258

376

Compound 327

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((2-(pyridin-3-yl)ethyl)amino)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



327

LC/MS: m/z calculated 718.5. found 719.5 (M+1)⁺

Example 259

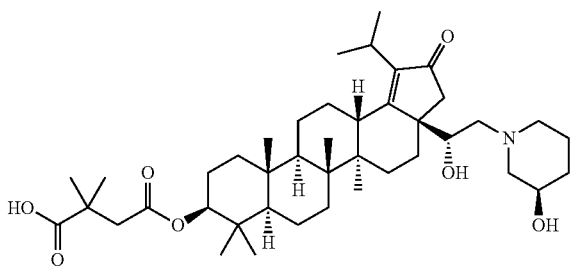
35

Compound 328

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((R)-3-hydroxypiperidin-1-yl)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

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328

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60

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LC/MS: m/z calculated 697.5. found 698.5 (M+1)⁺

377

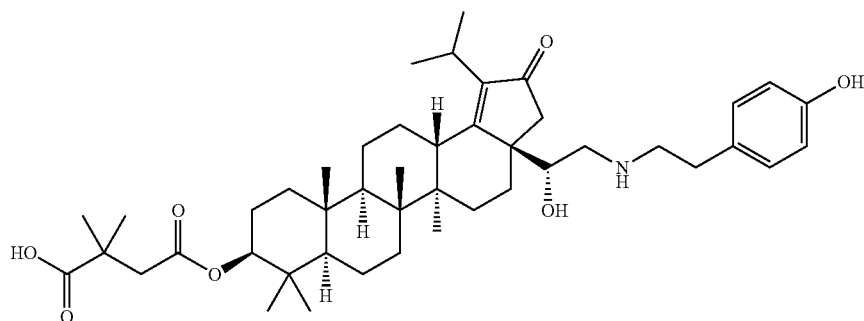
Example 260

378

Compound 329

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((4-hydroxyphenethyl)amino)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



329

LC/MS: m/z calculated 733.5. found 734.4 (M+1)⁺

35

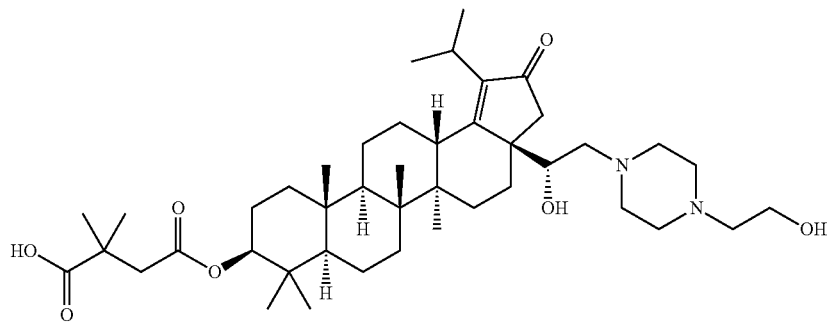
Example 261

Compound 330

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-(4-(2-hydroxyethyl)piperazin-1-yl)
 ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
 3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40

45



330

LC/MS: m/z calculated 726.5. found 727.5 (M+1)⁺

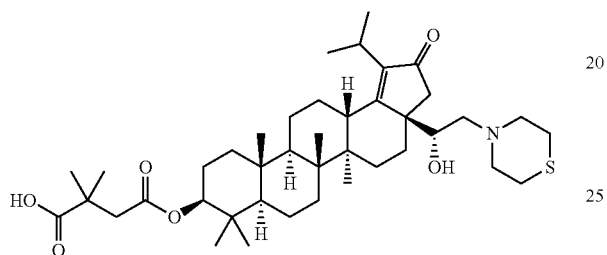
379

380

Example 262

Compound 331

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-thiomorpholinoethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

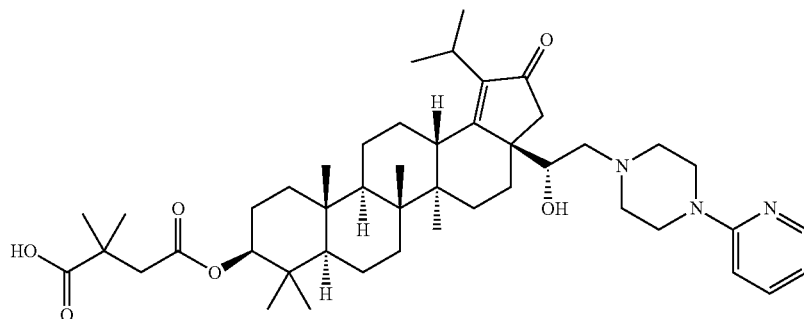


LC/MS: m/z calculated 699.4. found 700.4 (M+1)⁺

Example 263

Compound 332

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(4-(pyridin-2-yl)piperazin-1-yl)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 759.5. found 760.5 (M+1)⁺

381

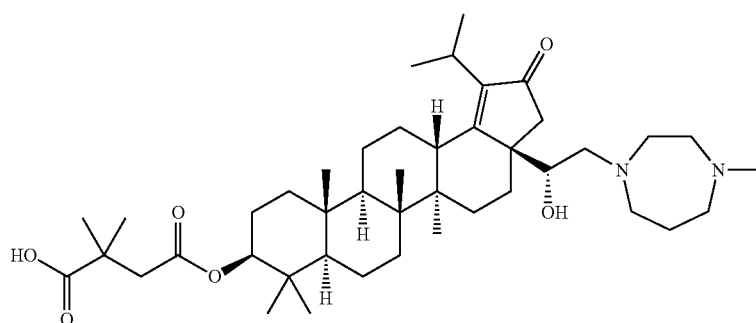
382

Example 264

Compound 333

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(4-methyl-1,4-diazepan-1-yl)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



333

LC/MS: m/z calculated 710.5. found 711.5 (M+1)⁺

35

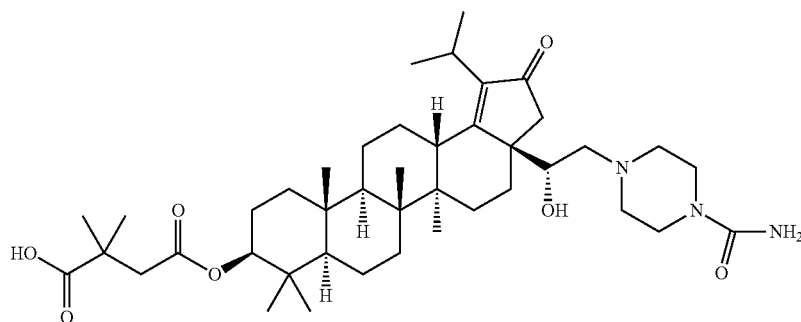
Example 265

Compound 334

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(4-carbamoylpiperidin-1-yl)-1-hydroxyethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



334

LC/MS: m/z calculated 724.5. found 725.5 (M+1)⁺

383

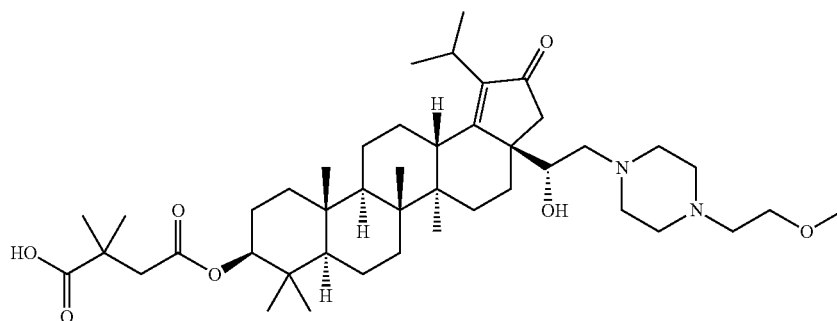
Example 266

384

Compound 335

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(4-(2-methoxyethyl)piperazin-1-
yl)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-
oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

5



335

LC/MS: m/z calculated 740.5. found 741.5 (M+1)⁺

35

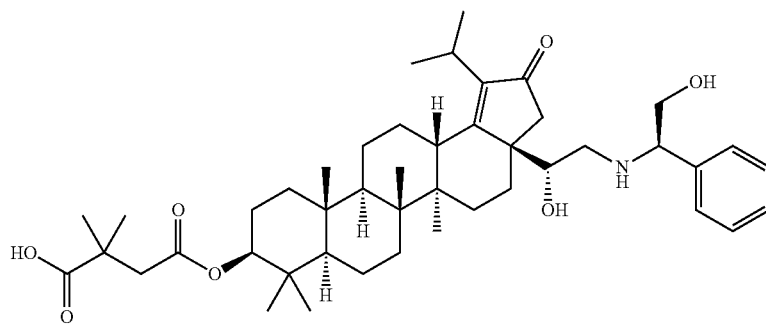
Example 267

Compound 336

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(((R)-2-hydroxy-1-phenylethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



336

LC/MS: m/z calculated 733.5. found 734.5 (M+1)⁺

385

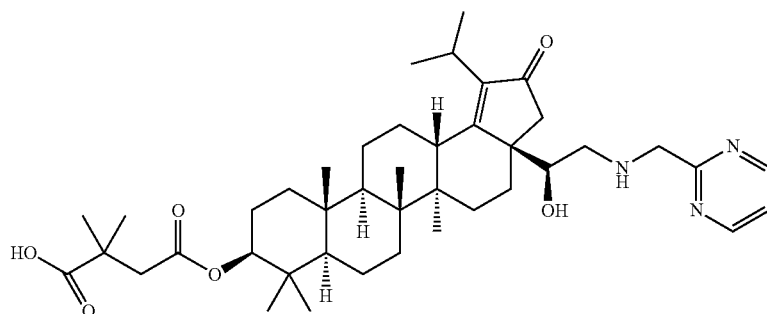
Example 268

386

Compound 337

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-((pyrimidin-2-ylmethyl)amino)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



337

LC/MS: m/z calculated 705.5. found 706.4 (M+1)⁺

35

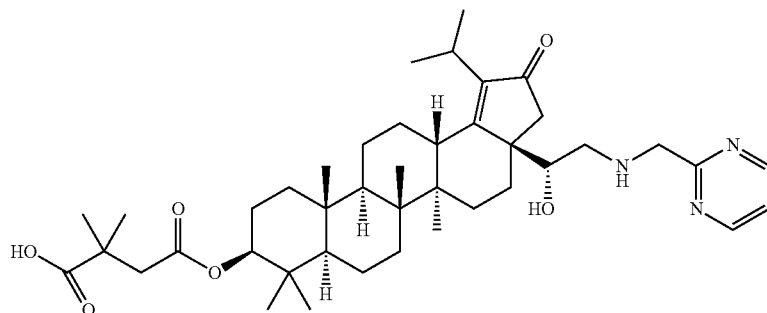
Example 269

Compound 338

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((pyrimidin-2-ylmethyl)amino)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



338

LC/MS: m/z calculated 705.5. found 706.4 (M+1)⁺

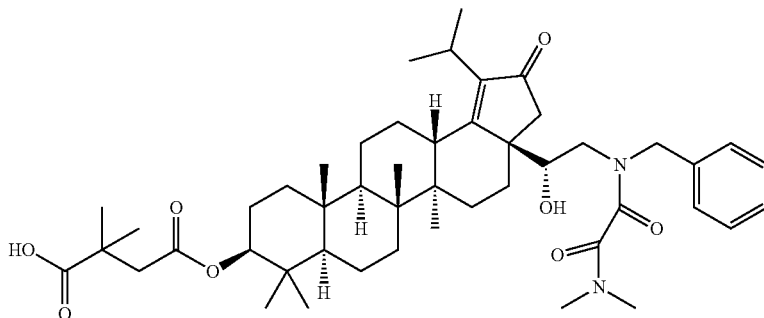
Example 270

Compound 339

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-benzyl-2-(dimethylamino)-2-oxoaceta-
mido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5

339



LC/MS: m/z calculated 802.5. found 803.5 (M+1)⁺

35

Example 271

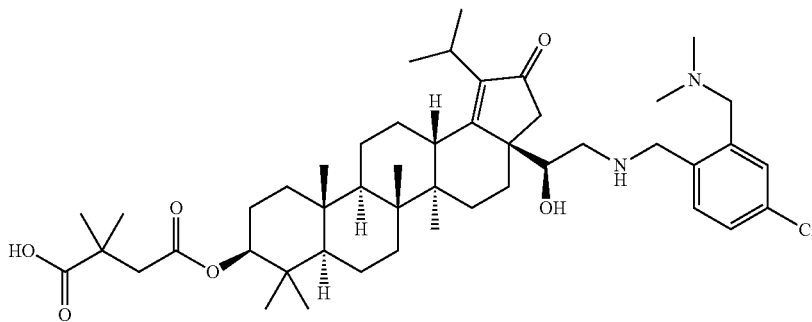
Compound 340

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chloro-2-((dimethylamino)methyl)benzyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45

340



LC/MS: m/z calculated 794.5. found 795.5 (M+1)⁺

389

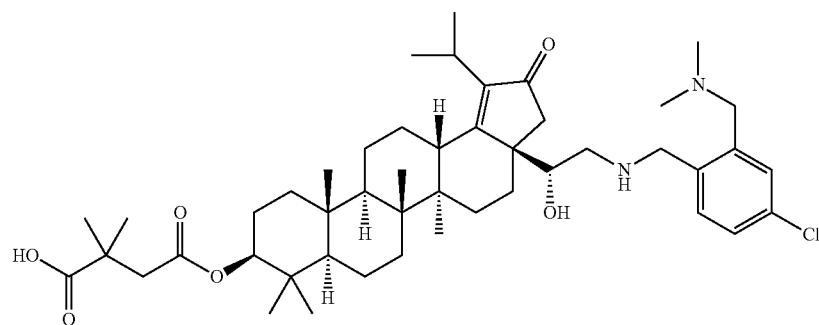
Example 272

390

Compound 341

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chloro-2-((dimethylamino)methyl)benzyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



341

LC/MS: m/z calculated 794.5. found 795.5 (M+1)⁺

35

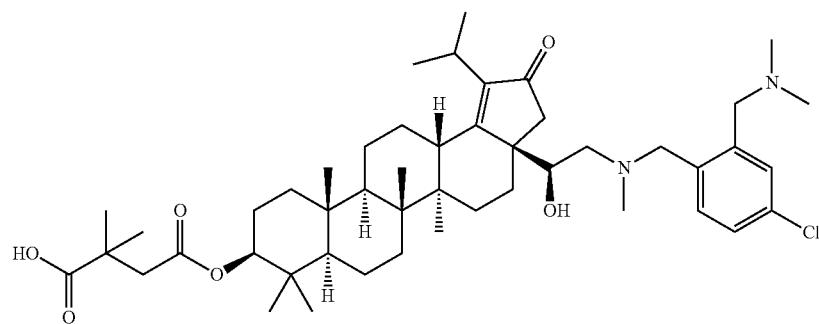
Example 273

Compound 342

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((4-chloro-2-((dimethylamino)methyl)benzyl)(me-
thyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

40

45



342

LC/MS: m/z calculated 808.5. found 809.5 (M+1)⁺

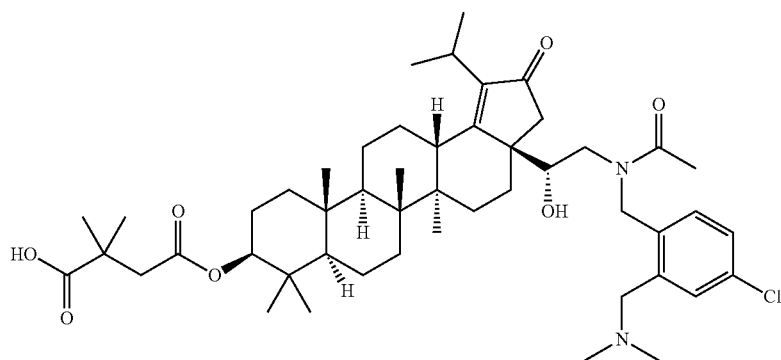
391

392

Example 274

Compound 343

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(4-chloro-2-((dimethylamino)methyl)ben-
zyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,
8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 5 10



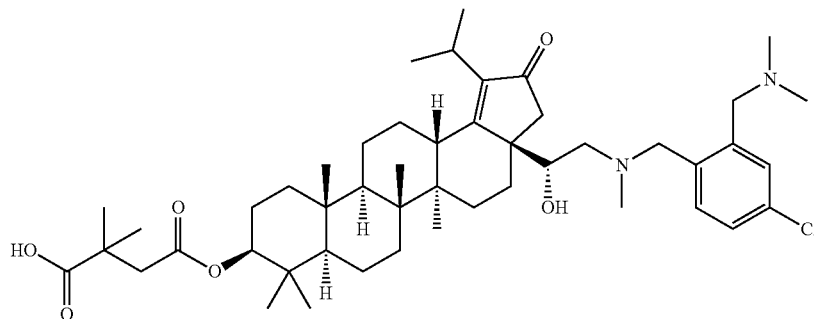
343

LC/MS: m/z calculated 836.5. found 837.5 (M+1)⁺

Example 275

Compound 344

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chloro-2-((dimethylamino)methyl)benzyl)
(methyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 40 45



344

LC/MS: m/z calculated 808.5. found 809.5 (M+1)⁺

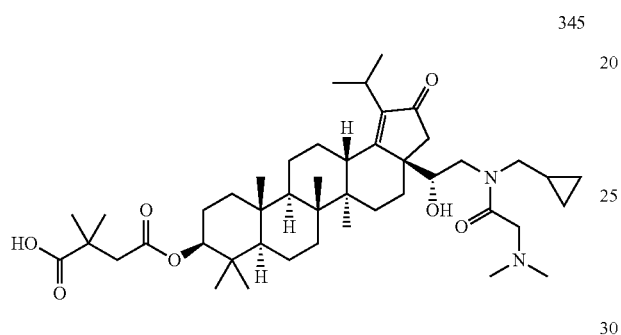
393

394

Example 276

Compound 345

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(N-(cyclopropylmethyl)-2-(dimethylamino)
 acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid

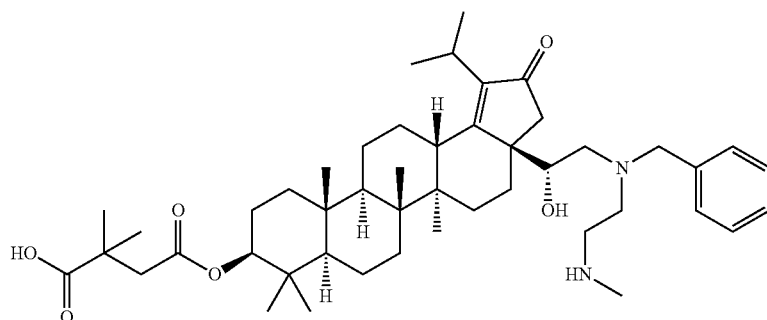


LC/MS: m/z calculated 752.5. found 753.5 (M+1)⁺

Example 277

Compound 346

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(benzyl(2-(methylamino)ethyl)amino)-1-hy-
 droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
 2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
 oxy)-2,2-dimethyl-4-oxobutanoic acid



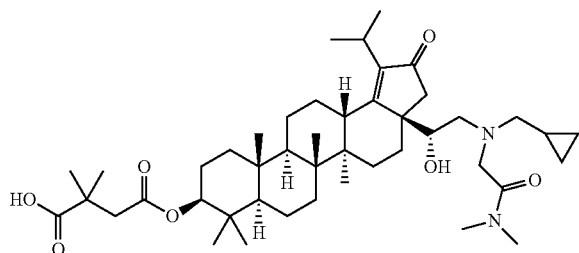
LC/MS: m/z calculated 760.5. found 761.5 (M+1)⁺

395

Example 278

Compound 347

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((cyclopropylmethyl)(2-(dimethylamino)-2-
oxoethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

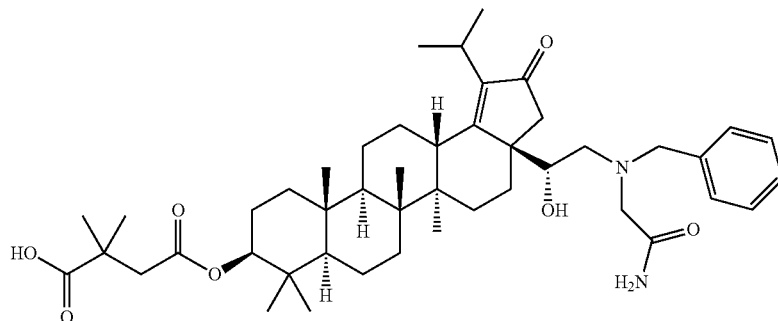
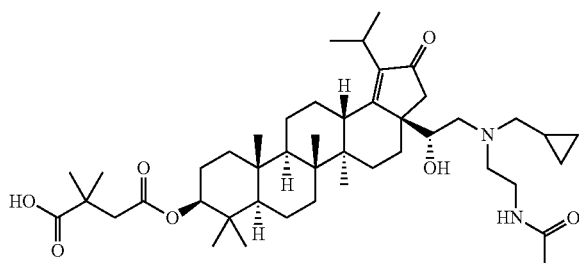


LC/MS: m/z calculated 752.5. found 753.5 (M+1)⁺

Example 279

Compound 348

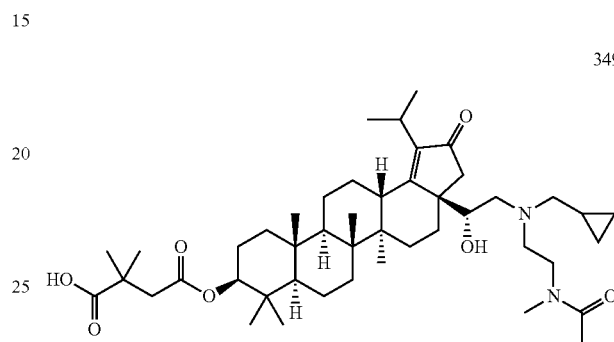
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-acetamidoethyl)(cyclopropylmethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

**396**LC/MS: m/z calculated 752.5. found 753.5 (M+1)⁺

Example 280

Compound 349

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((cyclopropylmethyl)(2-(N-methylacetamido)
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid



LC/MS: m/z calculated 766.5. found 767.5 (M+1)⁺

Example 281

Compound 350

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-amino-2-oxoethyl)(benzyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

350

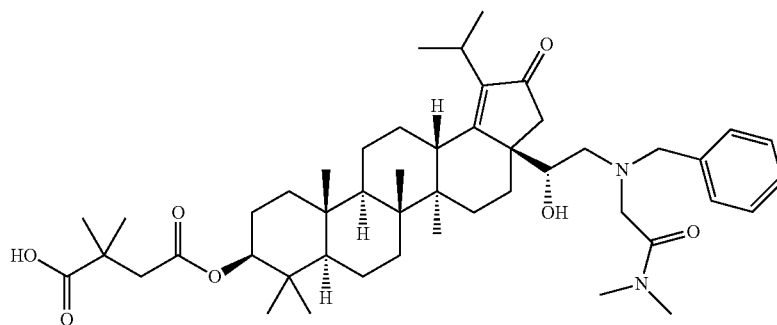
LC/MS: m/z calculated 760.5. found 761.5 (M+1)⁺

Example 282

Compound 351

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(benzyl(2-(dimethylamino)-2-oxoethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



351

LC/MS: m/z calculated 788.5. found 789.5 (M+1)⁺

35

Example 283

Compound 352

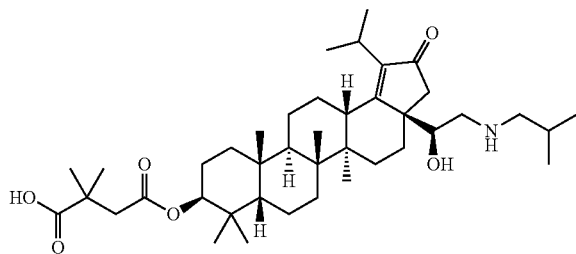
40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
1-hydroxy-2-(isobutylamino)ethyl)-1-isopropyl-5a,
5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

45

50

352



55

60

65

LC/MS: m/z calculated 669.5. found 670.5 (M+1)⁺

399

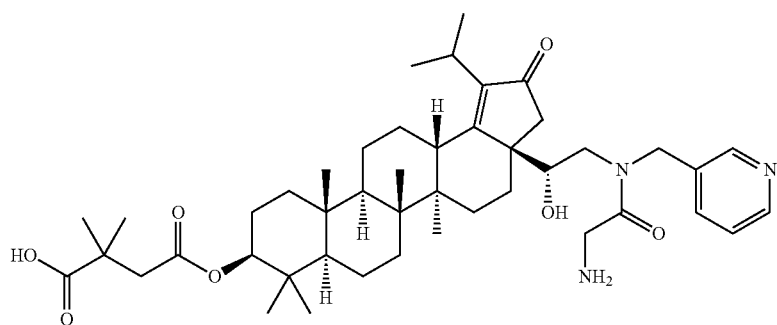
400

Example 284

Compound 353

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-amino-N-(pyridin-3-ylmethyl)acetamido)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



353

LC/MS: m/z calculated 761.5. found 762.5 (M+1)⁺

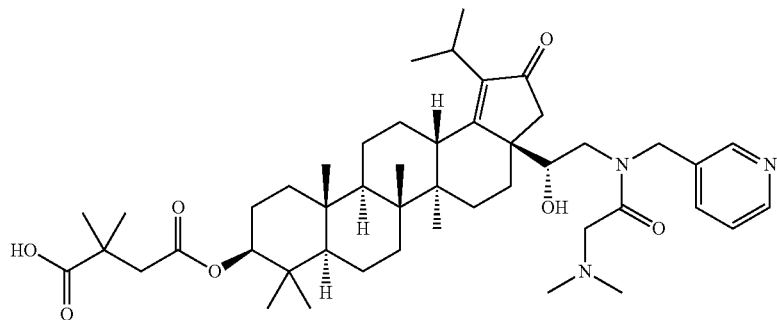
Example 285

35

Compound 354

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-(dimethylamino)-N-(pyridin-3-ylmethyl)
acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

40

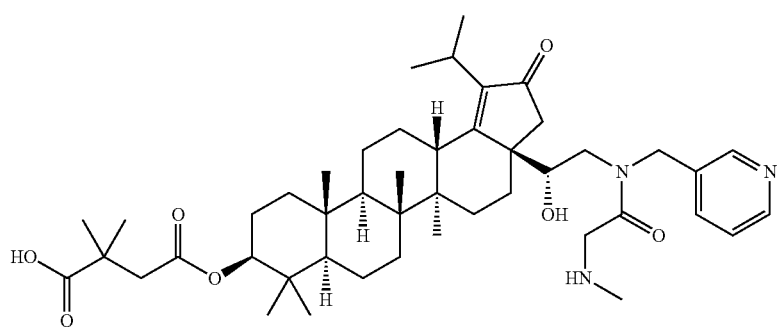


354

LC/MS: m/z calculated 789.5. found 790.5 (M+1)⁺

Compound 355

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-(2-(methylamino)-N-(pyridin-3-
 ylmethyl)acetamido)ethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid 5 10



355

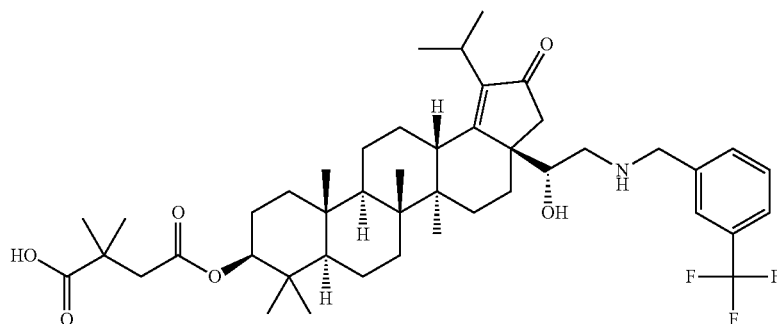
35

LC/MS: m/z calculated 775.5. found 776.5 (M+1)⁺

Example 287

Compound 356

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((3-(trifluoromethyl)benzyl)
 amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid 45



356

LC/MS: m/z calculated 771.5. found 772.4 (M+1)⁺

403

Example 288

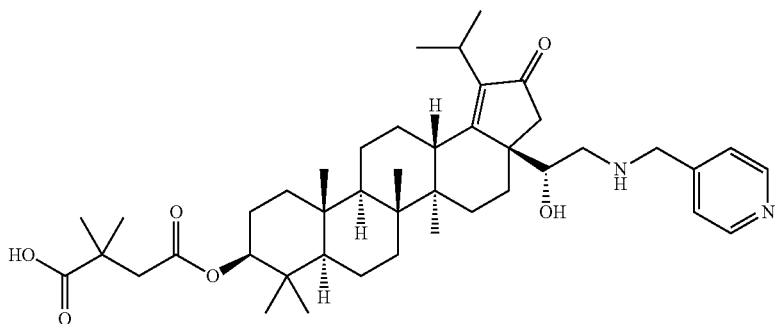
Compound 357

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((pyridin-4-ylmethyl)amino)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5

404

357



LC/MS: m/z calculated 704.5. found 705.5 (M+1)⁺

35

Example 290

Example 289

Compound 358

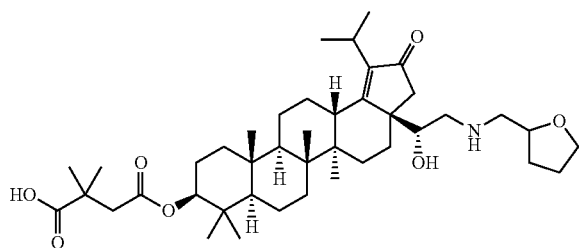
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((1R)-1-hydroxy-2-(((tetrahydrofuran-2-yl)methyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45

50

358



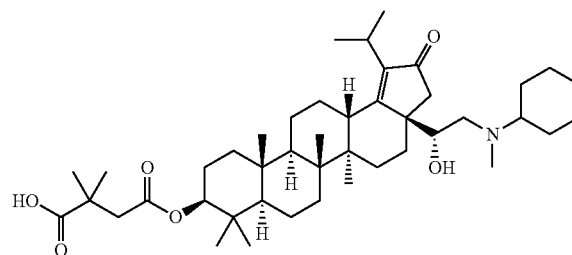
65

LC/MS: m/z calculated 697.5. found 698.5 (M+1)⁺

Compound 359

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(cyclohexyl(methyl)amino)-1-hydroxyethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

359



LC/MS: m/z calculated 709.5. found 710.5 (M+1)⁺

405

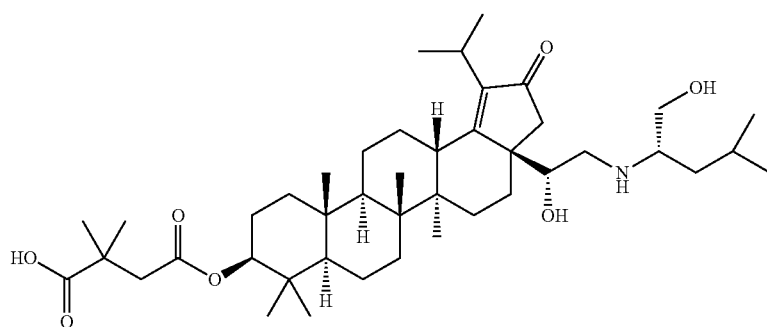
Example 291

406

Compound 360

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(((S)-1-hydroxy-4-methylpentan-
2-yl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pen-
tamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,
11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



360

LC/MS: m/z calculated 713.5. found 714.5 (M+1)⁺

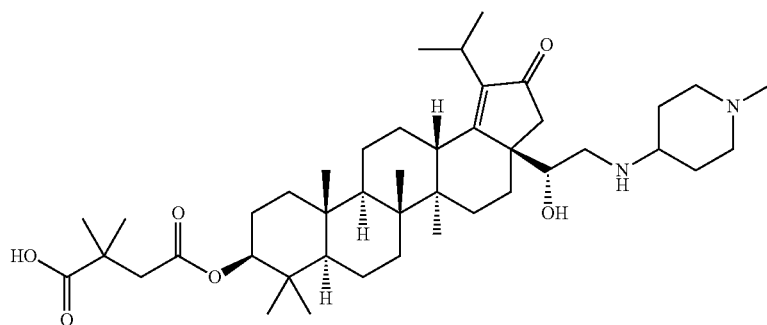
35

Example 292

Compound 361

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((1-methylpiperidin-4-yl)amino)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40



361

LC/MS: m/z calculated 710.5. found 711.5 (M+1)⁺

407

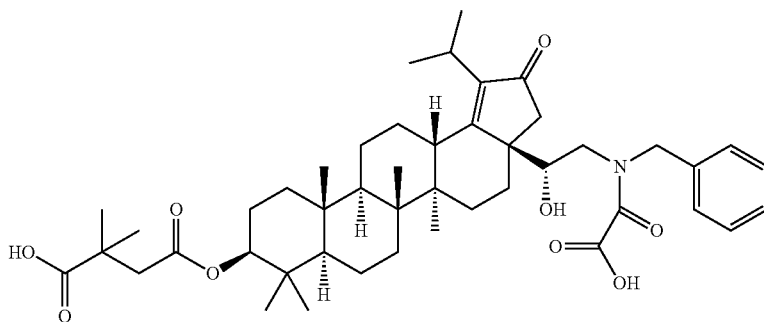
Example 293

408

Compound 362

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-benzyl-1-carboxyformamido)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



362

LC/MS: m/z calculated 775.5. found 776.5 (M+1)⁺

35

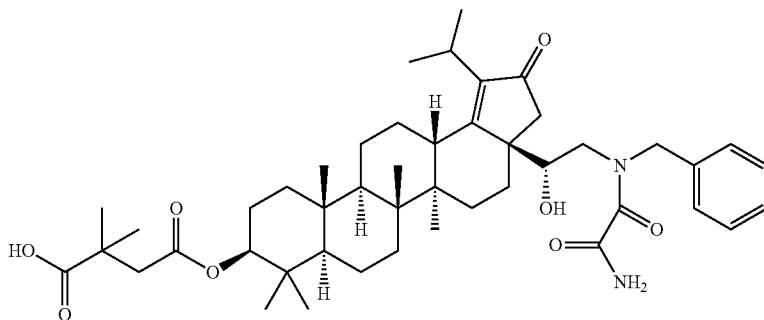
Example 294

Compound 363

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-amino-N-benzyl-2-oxoacetamido)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



363

LC/MS: m/z calculated 774.5. found 775.5 (M+1)⁺

409

410

Example 295

Compound 364

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(isobutylamino)ethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

10

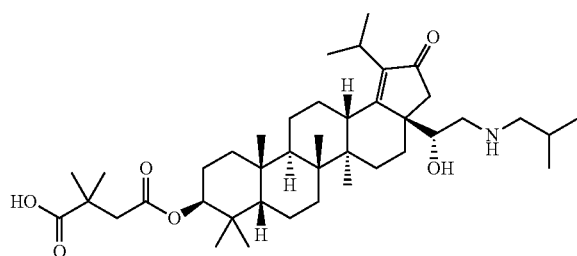
15

364

20

25

30



LC/MS: m/z calculated 669.5. found 670.5 (M+1)⁺

Example 296

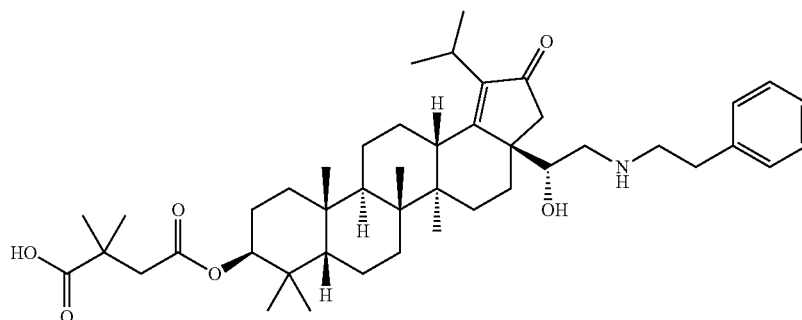
Compound 365

35

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(phenethylamino)ethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

365

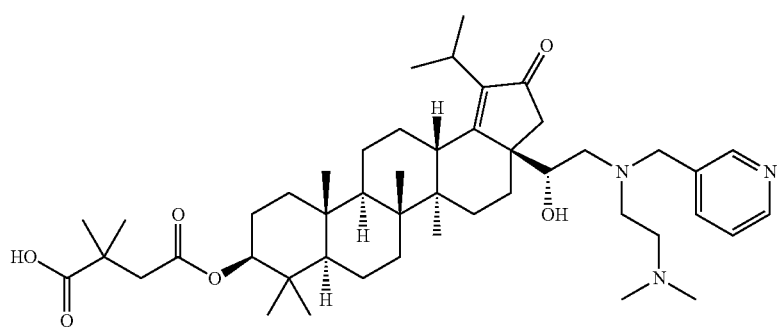


LC/MS: m/z calculated 717.5. found 718.5 (M+1)⁺

Example 297

Compound 366

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(pyridin-3-ylmethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid 5 10



366

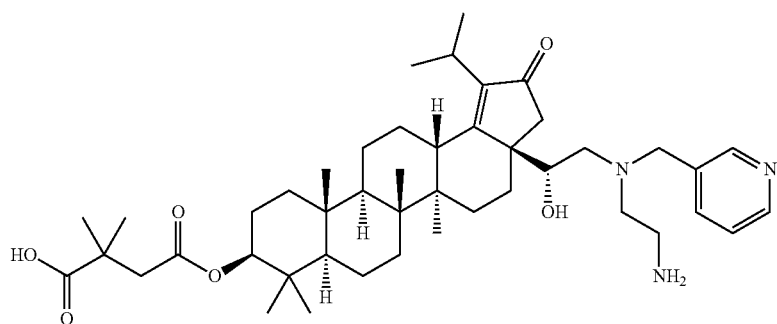
35

LC/MS: m/z calculated 775.5. found 776.5 (M+1)⁺

Example 298

Compound 367

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-aminoethyl)(pyridin-3-ylmethyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid 45



367

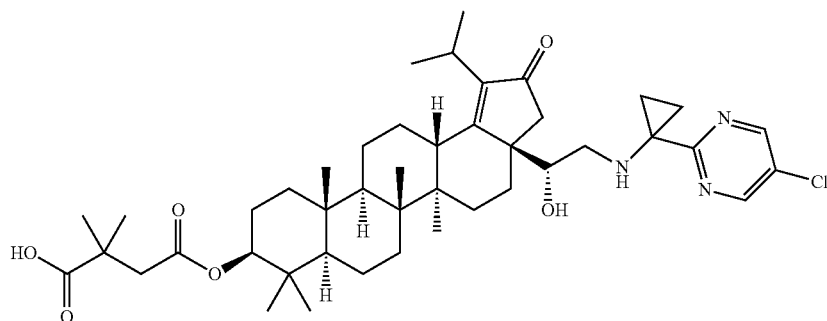
LC/MS: m/z calculated 747.5. found 748.5 (M+1)⁺

Example 299

Compound 368

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((1-(5-chloropyrimidin-2-yl)cyclopropyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



368

LC/MS: m/z calculated 765.5. found 766.5 (M+1)⁺

35

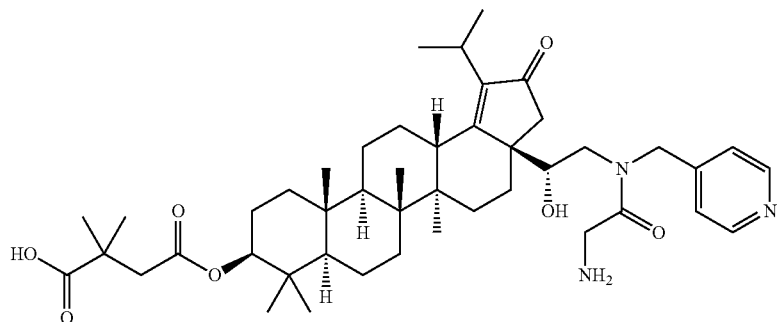
Example 300

Compound 369

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-amino-N-(pyridin-4-ylmethyl)acetamido)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



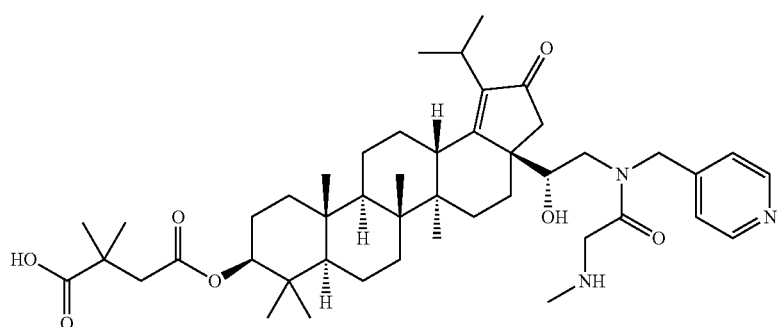
369

LC/MS: m/z calculated 761.5. found 762.5 (M+1)⁺

Example 301

Compound 370

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(2-(methylamino)-N-(pyridin-4-
ylmethyl)acetamido)ethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid 5 10



370

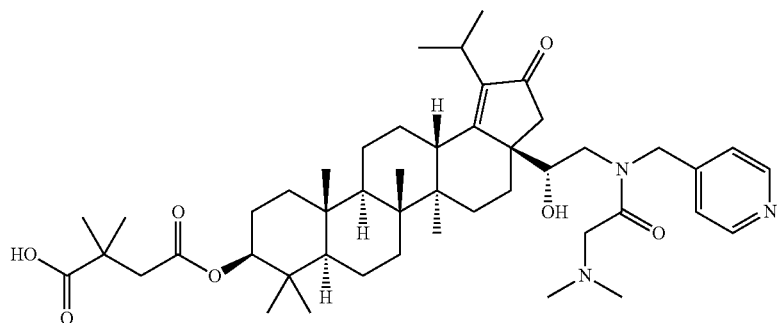
35

LC/MS: m/z calculated 775.5. found 776.5 (M+1)⁺

Example 302

Compound 371

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-(dimethylamino)-N-(pyridin-4-ylmethyl)
acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid 40 45



371

LC/MS: m/z calculated 789.5. found 790.5 (M+1)⁺

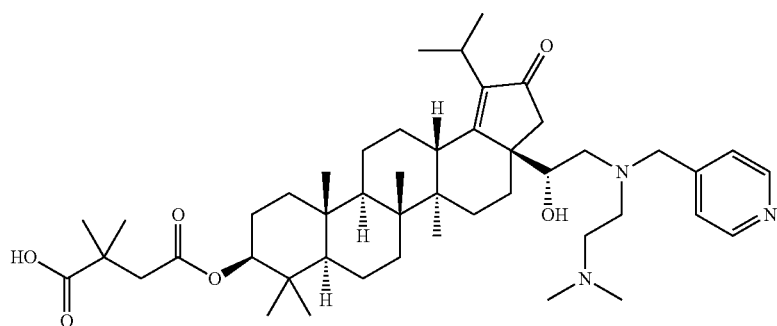
417

Example 303

418

Compound 372

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(pyridin-4-ylm-
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid 5 10



372

35

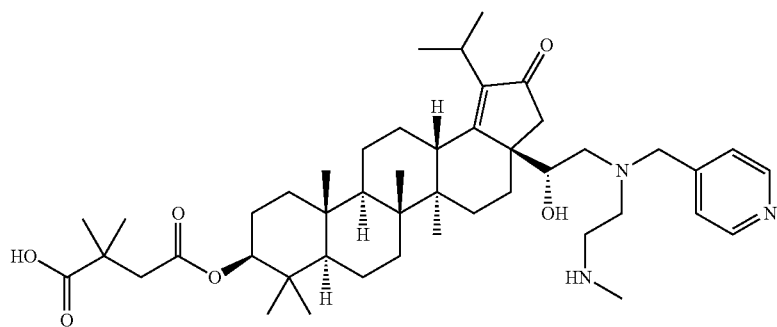
LC/MS: m/z calculated 775.5. found 776.5 (M+1)⁺

Example 304

Compound 373

40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((2-(methylamino)ethyl)(pyridin-
4-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid 45



373

LC/MS: m/z calculated 761.5. found 762.5 (M+1)⁺

419

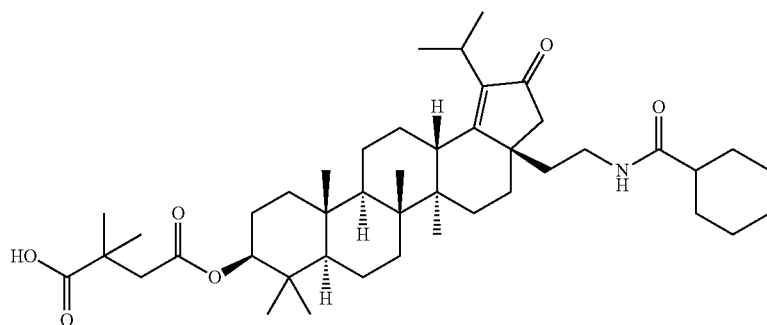
420

Example 305

Compound 374

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(cyclohexanecarboxamido)ethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5



374

LC/MS: m/z calculated 707.5. found 708.5 (M+1)⁺

35

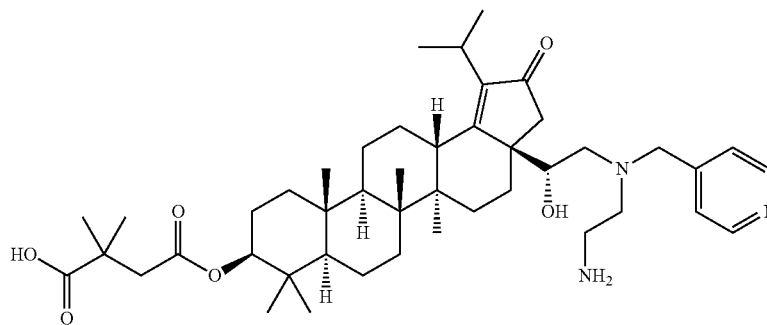
Example 306

Compound 375

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
(R)-2-((2-aminoethyl)(pyridin-4-ylmethyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



375

LC/MS: m/z calculated 747.5. found 748.5 (M+1)⁺

421

Example 307

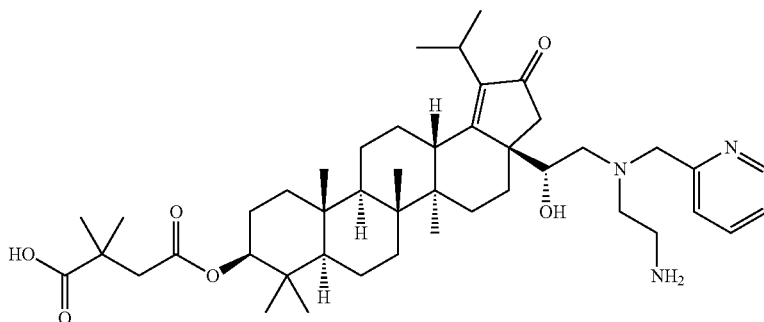
422

Compound 376

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-aminoethyl)(pyridin-2-ylmethyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5

376



LC/MS: m/z calculated 747.5. found 748.5 (M+1)⁺

35

Example 308

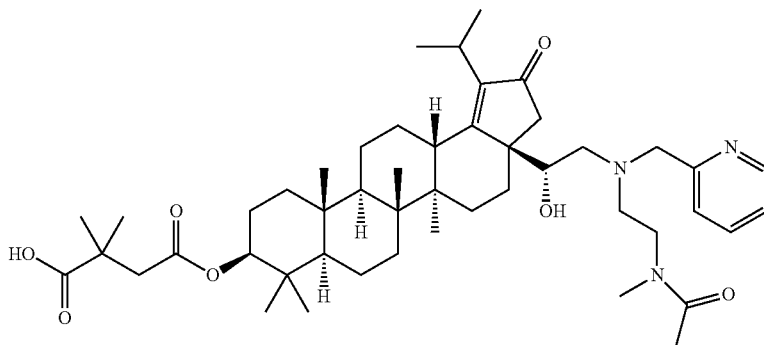
Compound 377

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((2-(N-methylacetamido)ethyl)
(pyridin-2-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

45

377



LC/MS: m/z calculated 803.5. found 804.5 (M+1)⁺

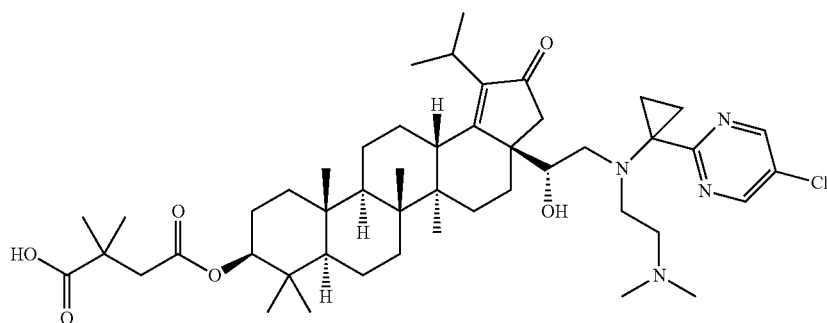
Example 309

Compound 378

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((1-(5-chloropyrimidin-2-yl)cyclopropyl)(2-
 (dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5

10



378

LC/MS: m/z calculated 836.5. found 837.5 (M+1)⁺

35

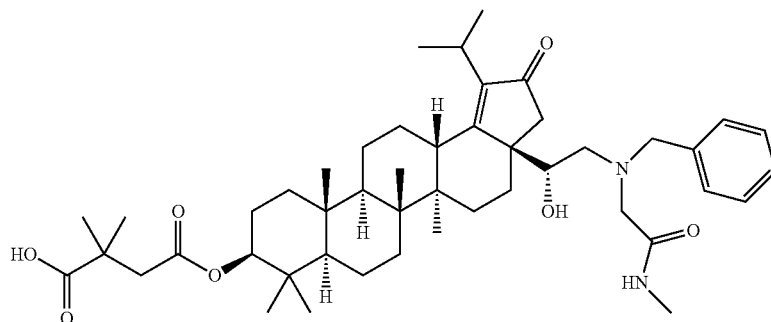
Example 310

Compound 379

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(benzyl(2-(methylamino)-2-oxoethyl)amino)-
 1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



379

LC/MS: m/z calculated 774.5. found 775.5 (M+1)⁺

425

Example 311

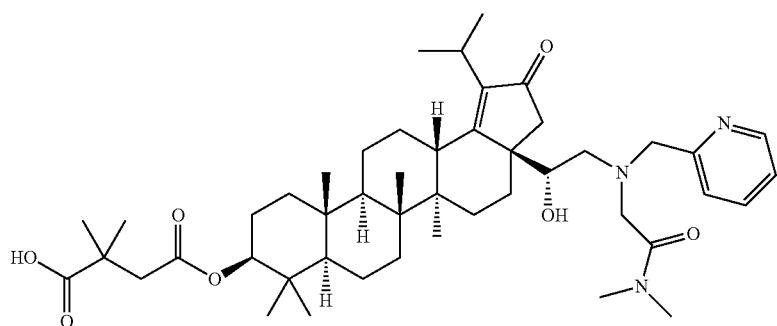
426

Compound 380

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((2-(dimethylamino)-2-oxoethyl)(pyridin-2-
 ylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,
 8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
 10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid

5

10



380

LC/MS: m/z calculated 789.5. found 790.5 (M+1)⁺

35

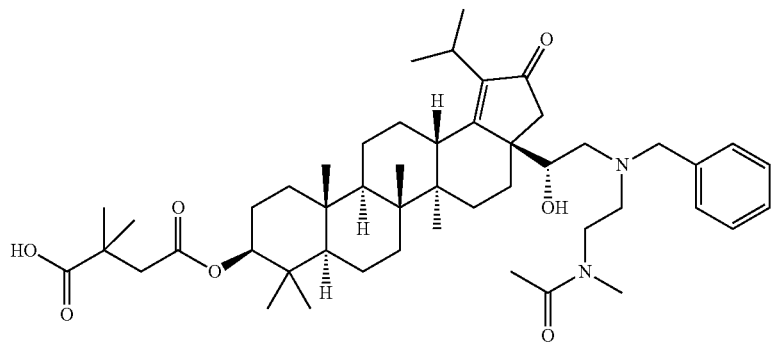
Example 312

Compound 381

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(benzyl(2-(N-methylacetamido)ethyl)amino)-
 1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



381

LC/MS: m/z calculated 802.5. found 803.5 (M+1)⁺

427

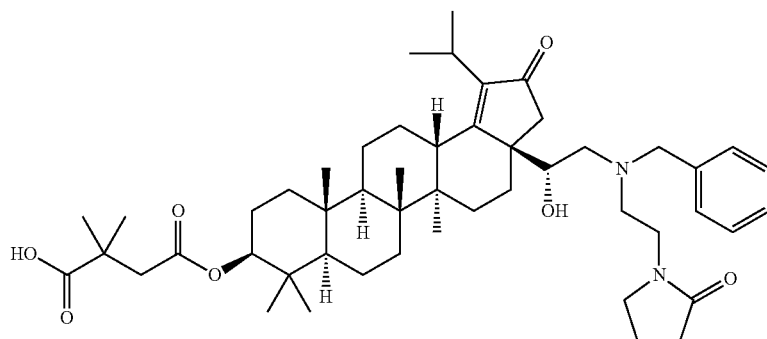
Example 313

428

Compound 382

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(benzyl(2-(2-oxopyrrolidin-1-yl)ethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



382

LC/MS: m/z calculated 814.5. found 815.5 (M+1)⁺

35

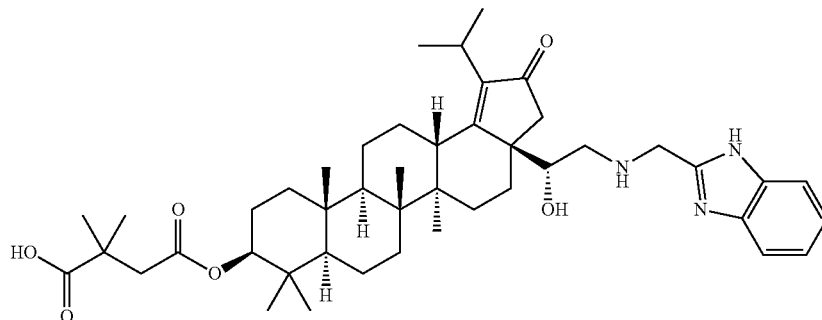
Example 314

Compound 383

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((1H-benzo[d]imidazol-2-yl)methyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



383

LC/MS: m/z calculated 743.5. found 744.5 (M+1)⁺

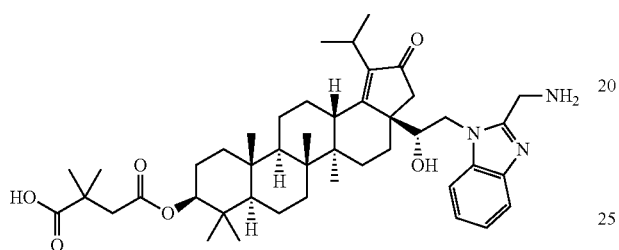
429

430

Example 315

Compound 384

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-(aminomethyl)-1H-benzo[d]imidazol-1-
yl)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pen-
tamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,
11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

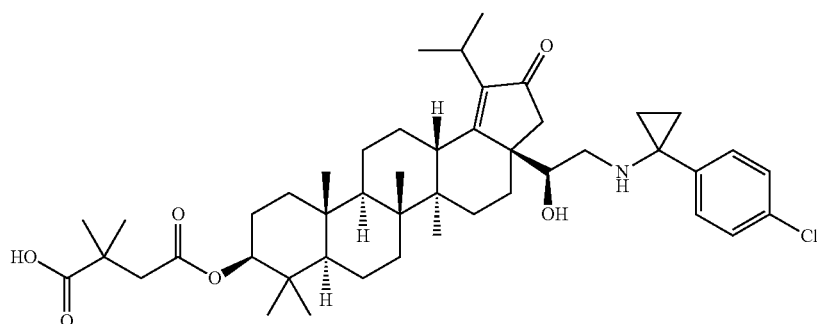


LC/MS: m/z calculated 743.5. found 744.5 (M+1)⁺

Example 316

Compound 385

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((1-(4-chlorophenyl)cyclopropyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 763.5. found 764.5 (M+1)⁺

431

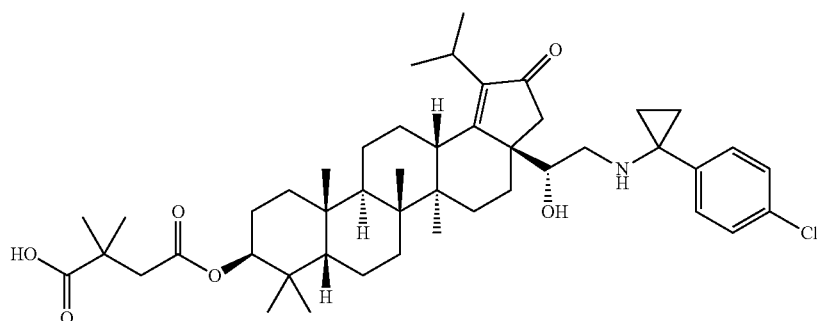
Example 317

432

Compound 386

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((1-(4-chlorophenyl)cyclopropyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



386

LC/MS: m/z calculated 763.5. found 764.5 (M+1)⁺

35

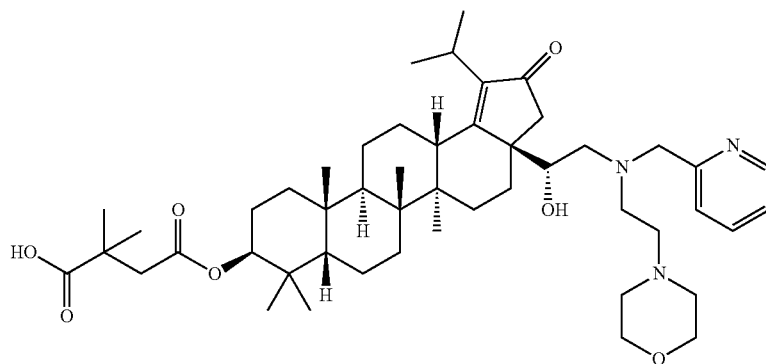
Example 318

Compound 387

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((2-morpholinoethyl)(pyridin-2-
ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



387

LC/MS: m/z calculated 817.6. found 818.5 (M+1)⁺

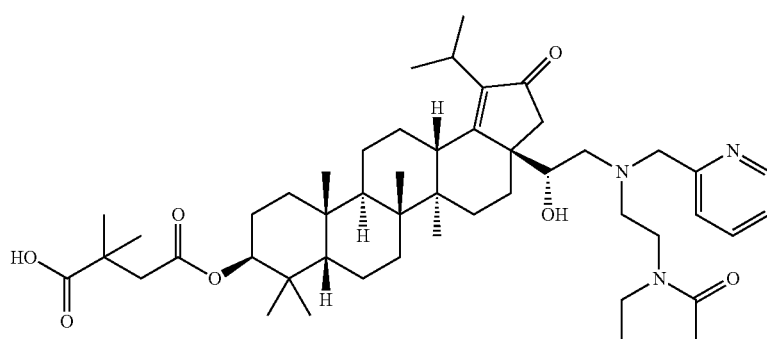
Example 319

Compound 388

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((2-(2-oxopyrrolidin-1-yl)ethyl)
 (pyridin-2-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,
 8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
 10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid

5

10



388

LC/MS: m/z calculated 815.5. found 816.5 (M+1)⁺

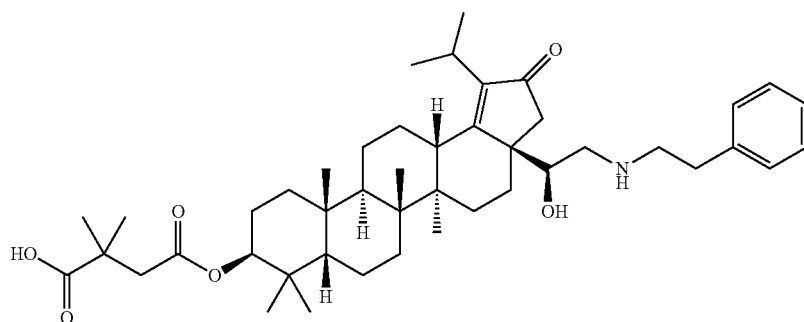
Example 320

Compound 389

40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
 1-hydroxy-2-(phenethylamino)ethyl)-1-isopropyl-5a,
 5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
 8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid

45



389

LC/MS: m/z calculated 717.5. found 718.5 (M+1)⁺

435

436

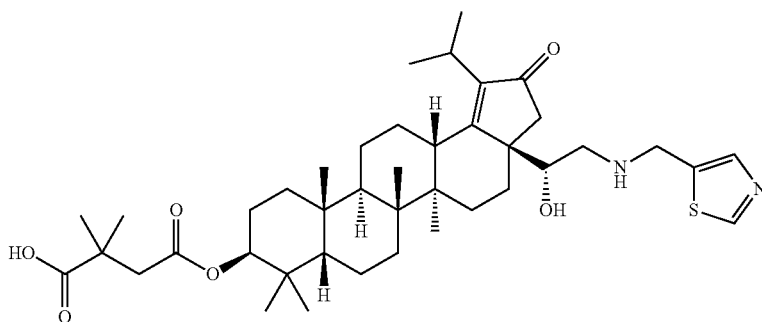
Example 321

Compound 390

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((thiazol-5-ylmethyl)amino)ethyl)-
 1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
 5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5

390



LC/MS: m/z calculated 710.4. found 711.4 (M+1)⁺

Example 322

40

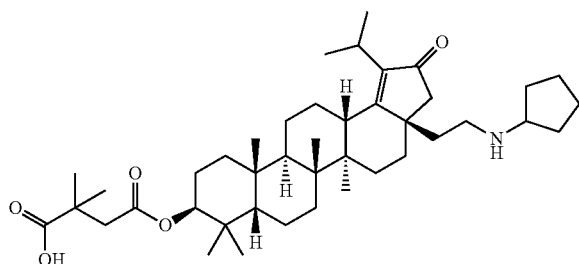
Compound 391

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 (cyclopentylamino)ethyl)-1-isopropyl-5a,5b,8,8,11a-
 pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
 11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
 chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

45

50

391



55

60

65

LC/MS: m/z calculated 665.5. found 666.5 (M+1)⁺

437

438

Example 323

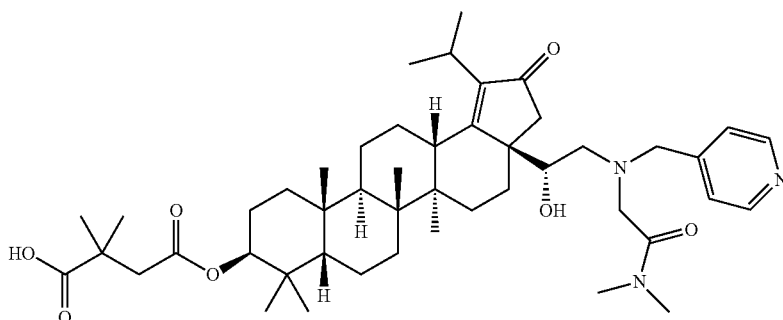
Compound 392

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((2-(dimethylamino)-2-oxoethyl)(pyridin-4-
 ylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,
 8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
 10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid

5

10

392



LC/MS: m/z calculated 789.5. found 790.5 (M+1)⁺

Example 324

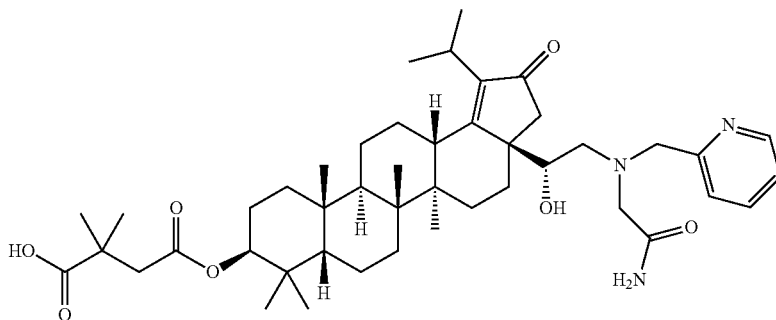
35

Compound 393

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((2-amino-2-oxoethyl)(pyridin-2-ylmethyl)
 amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
 pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
 11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
 chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

393



LC/MS: m/z calculated 761.5. found 762.5 (M+1)⁺

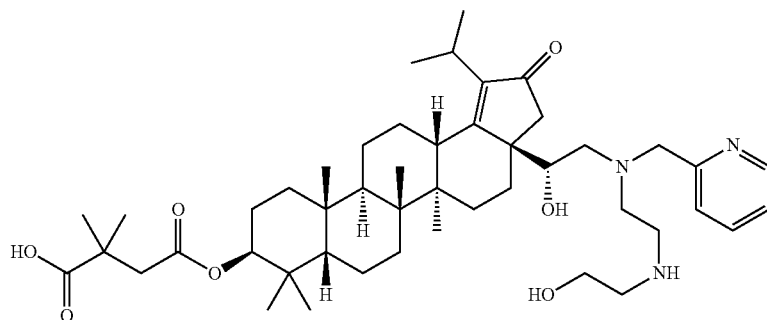
439

440

Example 325

Compound 394

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((2-((2-hydroxyethyl)amino)ethyl)
(pyridin-2-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 5 10



394

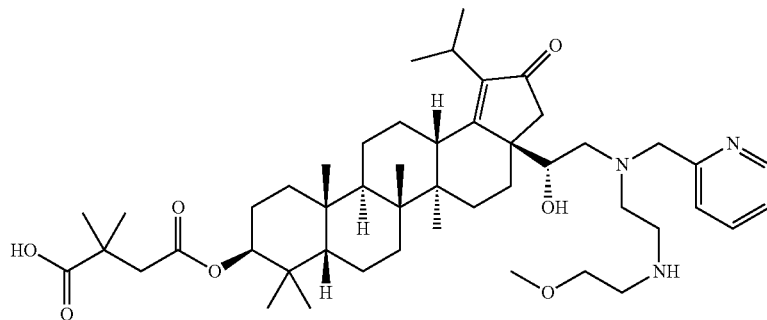
LC/MS: m/z calculated 791.5. found 792.5 (M+1)⁺

35

Example 326

Compound 395

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((2-((2-methoxyethyl)amino)ethyl)
(pyridin-2-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 40 45



395

LC/MS: m/z calculated 805.6. found 806.5 (M+1)⁺

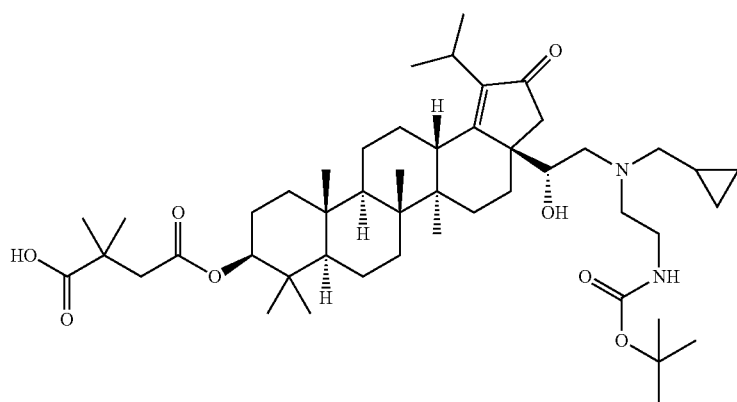
441

Example 327

442

Compound 396

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-((tert-butoxycarbonyl)amino)ethyl)(cyclo-
propylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 5 10



396

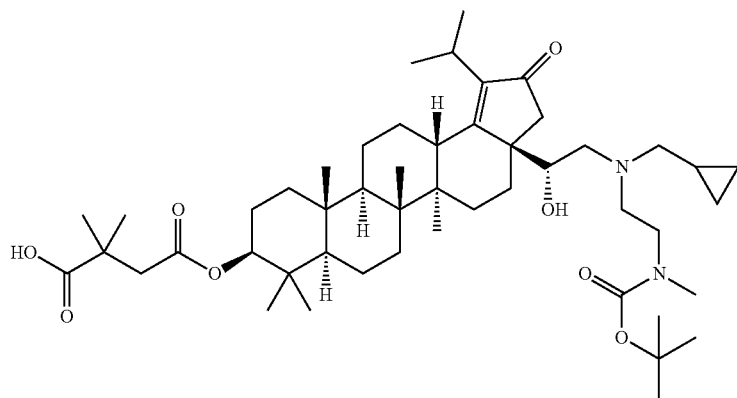
LC/MS: m/z calculated 810.6. found 811.5 (M+1)⁺

Example 328

35

Compound 397

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-((tert-butoxycarbonyl)(methyl)amino)
ethyl)(cyclopropylmethyl)amino)-1-hydroxyethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid 40 45



397

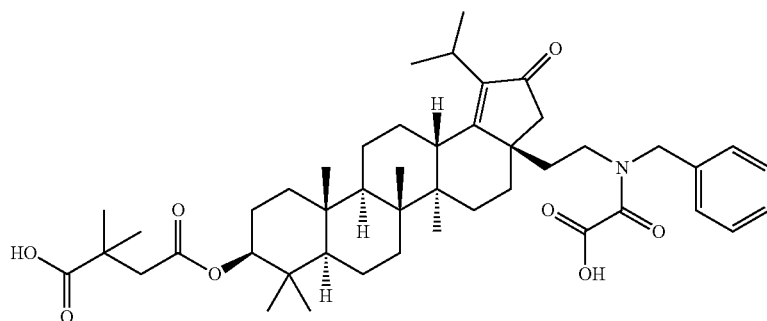
LC/MS: m/z calculated 824.6. found 825.5 (M+1)⁺

Example 329

Compound 398

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-(N-benzyl-1-carboxyformamido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



398

LC/MS: m/z calculated 759.5. found 760.5 (M+1)⁺

35

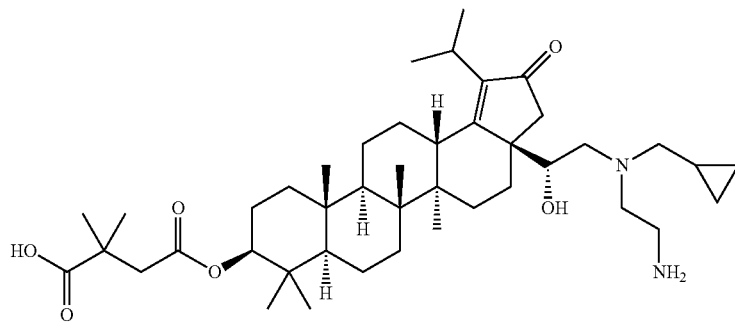
Example 330

Compound 399

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-aminoethyl)(cyclopropylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,4a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



399

LC/MS: m/z calculated 710.5. found 711.5 (M+1)⁺

445

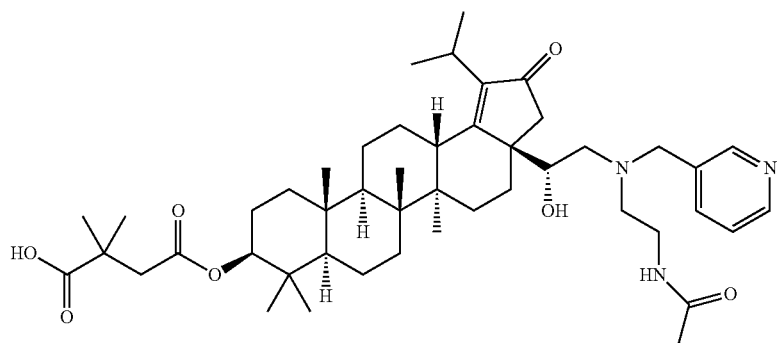
Example 331

446

Compound 400

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-acetamidoethyl)(pyridin-3-ylmethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



400

LC/MS: m/z calculated 789.5. found 790.5 (M+1)⁺

35

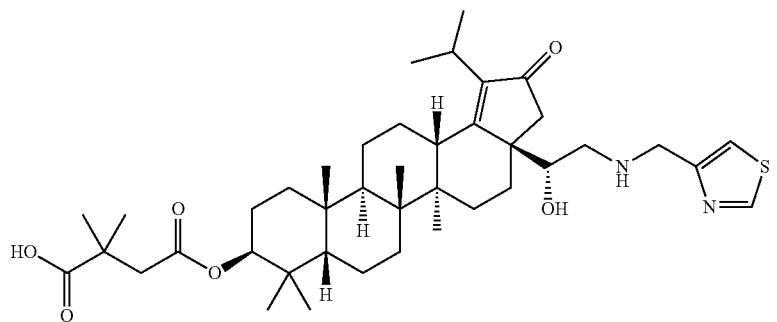
Example 332

Compound 401

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((thiazol-4-ylmethyl)amino)ethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



401

LC/MS: m/z calculated 710.4. found 711.4 (M+1)⁺

447

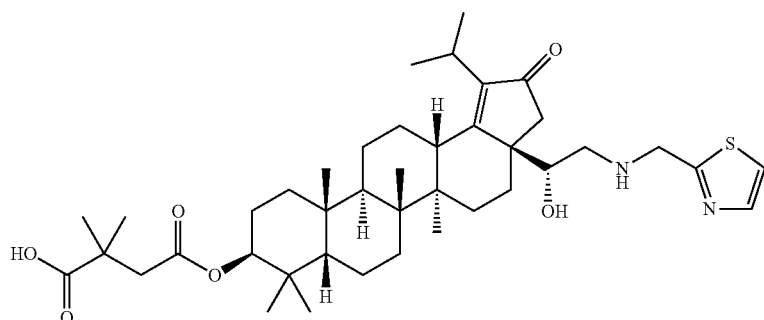
Example 333

448

Compound 402

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((thiazol-2-ylmethyl)amino)ethyl)-
 1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
 5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5



402

LC/MS: m/z calculated 710.4. found 711.4 (M+1)⁺

35

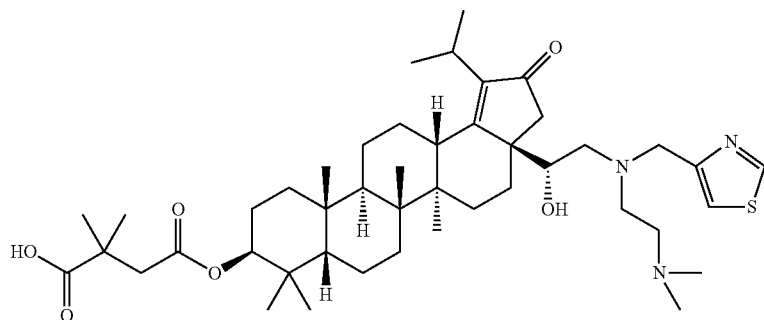
Example 334

Compound 403

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((2-(dimethylamino)ethyl)(thiazol-4-ylm-
 ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid

40

45



403

LC/MS: m/z calculated 781.5. found 782.5 (M+1)⁺

449

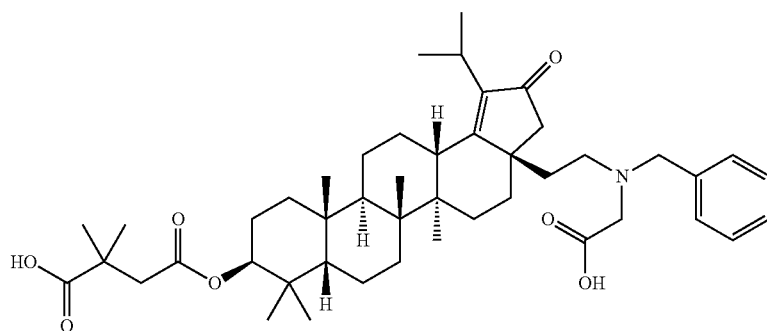
450

Example 335

Compound 404

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(benzyl(carboxymethyl)amino)ethyl)-1-isopropyl-5a,
5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5



404

LC/MS: m/z calculated 745.5. found 746.5 (M+1)⁺

35

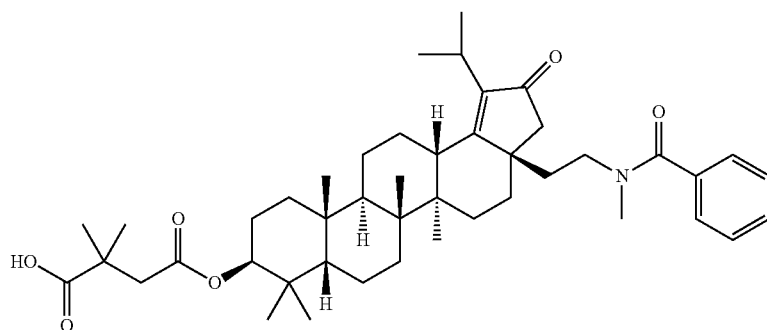
Example 336

Compound 405

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-3a-(2-(N-methyl-
benzamido)ethyl)-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

45



405

LC/MS: m/z calculated 715.5. found 716.5 (M+1)⁺

451

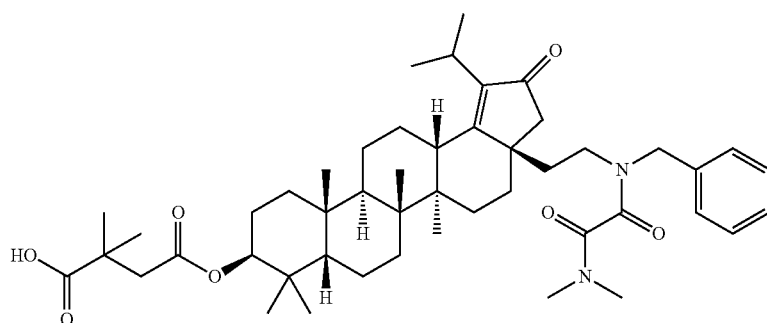
Example 337

452

Compound 406

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(N-benzyl-2-(dimethylamino)-2-oxoacetamido)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



406

LC/MS: m/z calculated 786.5. found 787.5 (M+1)⁺

35

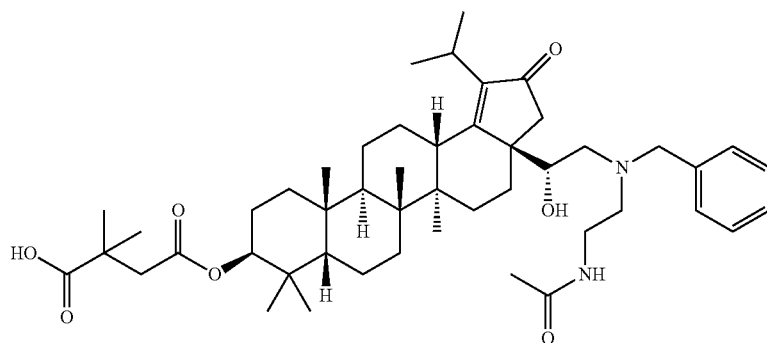
Example 338

Compound 407

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-acetamidoethyl)(benzyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



407

LC/MS: m/z calculated 788.5. found 789.5 (M+1)⁺

453

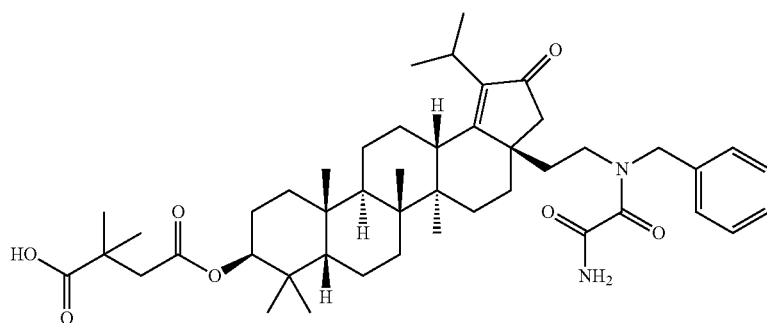
454

Example 339

Compound 408

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(2-amino-N-benzyl-2-oxoacetamido)ethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5



408

LC/MS: m/z calculated 758.5. found 759.5 (M+1)⁺

35

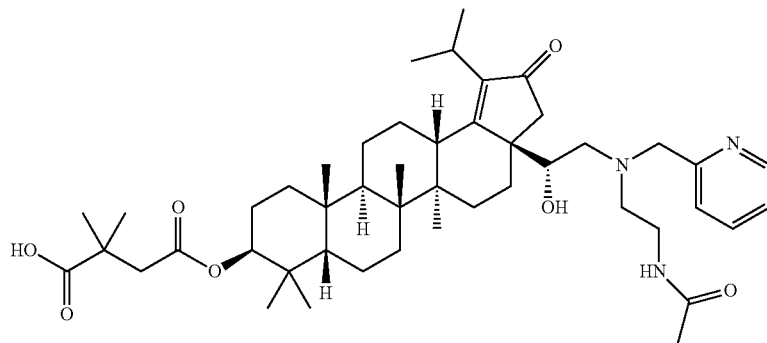
Example 340

Compound 409

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-acetamidoethyl)(pyridin-2-ylmethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



409

LC/MS: m/z calculated 789.5. found 790.5 (M+1)⁺

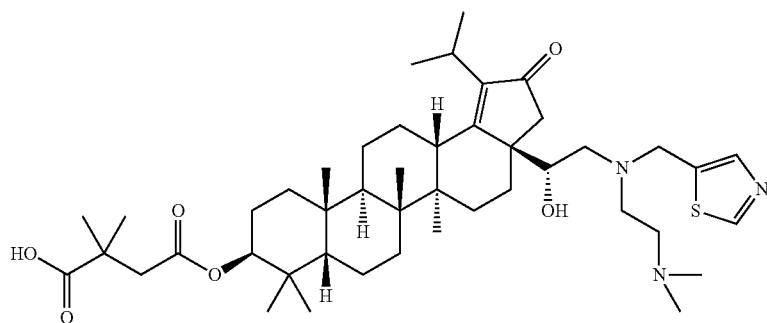
455

Example 341

456

Compound 410

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(thiazol-5-ylm-
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid 10



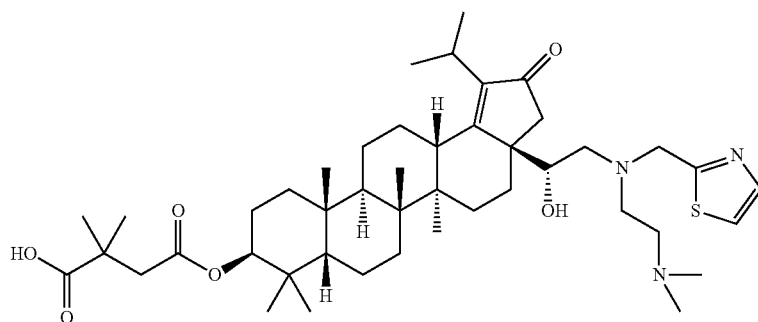
410

LC/MS: m/z calculated 781.5. found 782.5 (M+1)⁺ 35

Example 342

Compound 411

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(thiazol-2-ylm-
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid 45



411

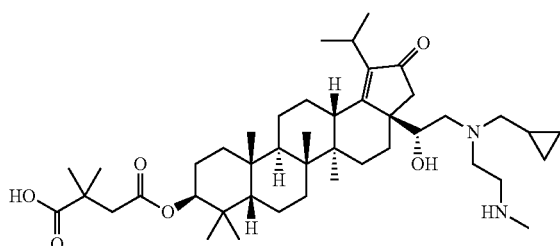
LC/MS: m/z calculated 781.5. found 782.5 (M+1)⁺

457

Example 343

Compound 412

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((cyclopropylmethyl)(2-(methylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

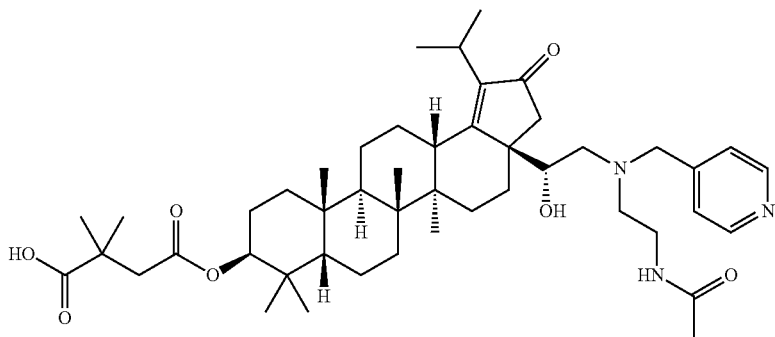


LC/MS: m/z calculated 724.5. found 725.5 (M+1)⁺

Example 344

Compound 413

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-acetamidoethyl)(pyridin-4-ylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



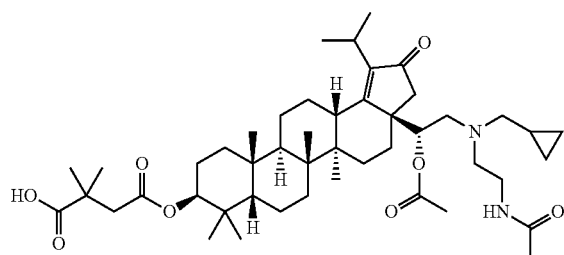
LC/MS: m/z calculated 789.5. found 790.5 (M+1)⁺

458

Example 345

Compound 414

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-acetamidoethyl)(cyclopropylmethyl)amino)-1-acetoxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

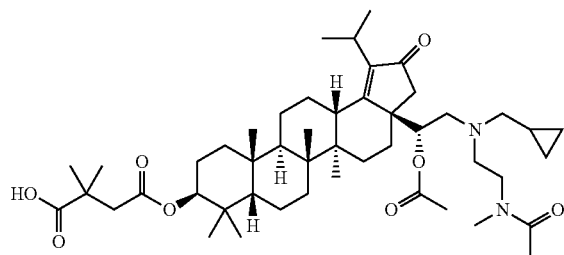


LC/MS: m/z calculated 794.5. found 795.5 (M+1)⁺

Example 346

Compound 415

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-acetoxy-2-((cyclopropylmethyl)(2-(N-methylacetamido)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 808.6. found 809.5 (M+1)⁺

413

459

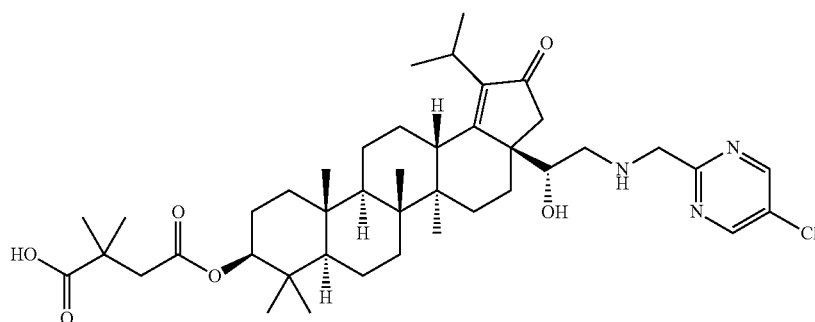
Example 347

460

Compound 416

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((5-chloropyrimidin-2-yl)methyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



416

LC/MS: m/z calculated 739.4. found 740.4 (M+1)⁺

35

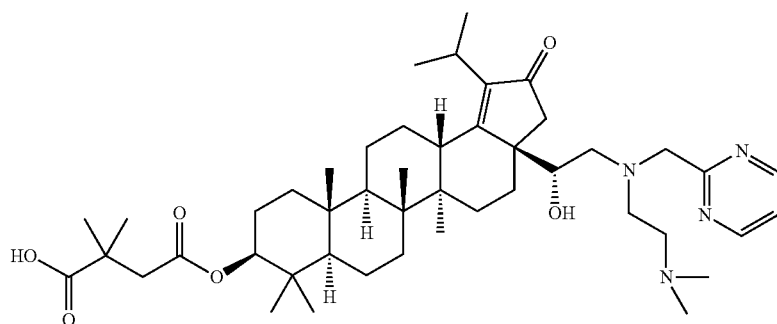
Example 348

Compound 417

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(pyrimidin-2-ylm-
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

40

45



417

LC/MS: m/z calculated 776.5. found 777.5 (M+1)⁺

461

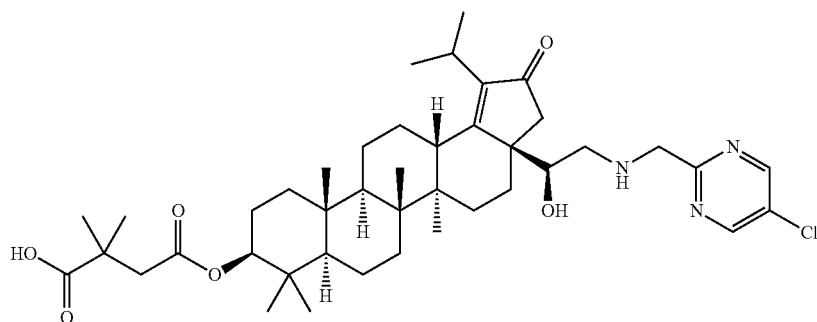
Example 349

462

Compound 418

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(((5-chloropyrimidin-2-yl)methyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

5



418

LC/MS: m/z calculated 739.4. found 740.4 (M+1)⁺

35

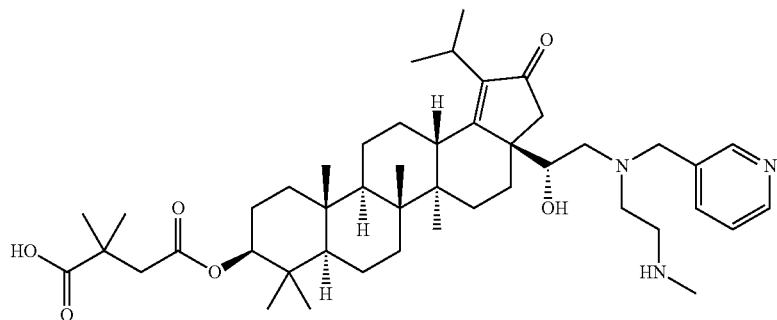
Example 350

Compound 419

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((2-(methylamino)ethyl)(pyridin-
3-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



419

LC/MS: m/z calculated 761.5. found 762.5 (M+1)⁺

463

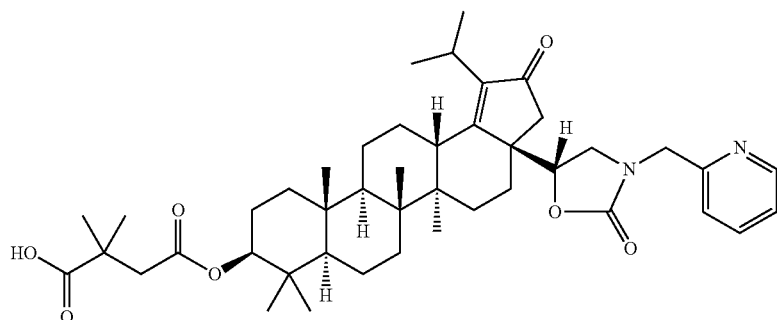
Example 351

464

Compound 420

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-((R)-2-
oxo-3-(pyridin-2-ylmethyl)oxazolidin-5-yl)-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



420

LC/MS: m/z calculated 730.5. found 731.4 (M+1)⁺

35

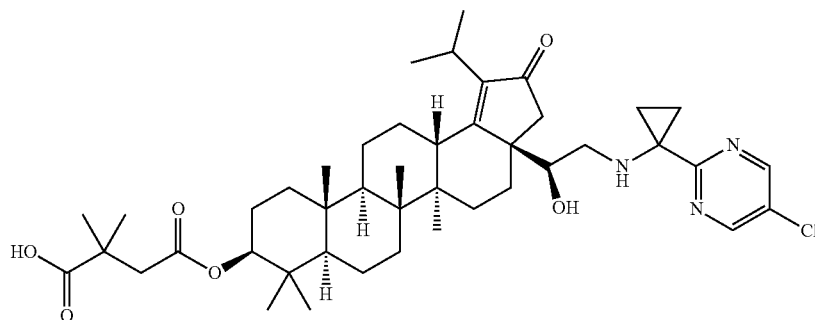
Example 352

Compound 421

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((1-(5-chloropyrimidin-2-yl)cyclopropyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



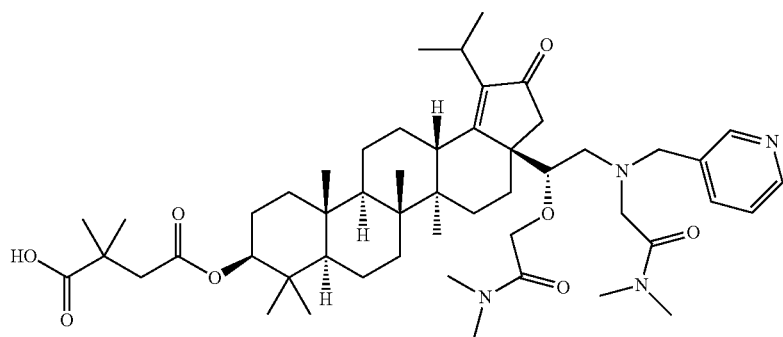
421

LC/MS: m/z calculated 765.4. found 766.4 (M+1)⁺

Example 353

Compound 422

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2,11-dimethyl-3,10-dioxo-5-(pyridin-3-ylm-
 ethyl)-8-oxa-2,5,11-triazadodecan-7-yl)-1-isopropyl-
 5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,
 7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid 5 10



422

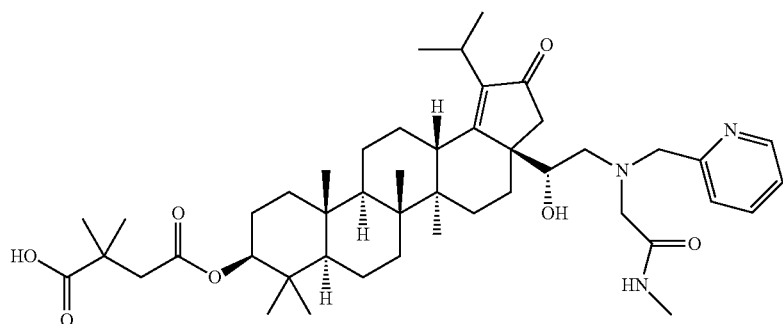
35

LC/MS: m/z calculated 874.6. found 875.6 (M+1)⁺

Example 354

Compound 423

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((2-(methylamino)-2-oxoethyl)
 (pyridin-2-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,
 8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
 10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid 45



423

LC/MS: m/z calculated 775.5. found 776.5 (M+1)⁺

467

468

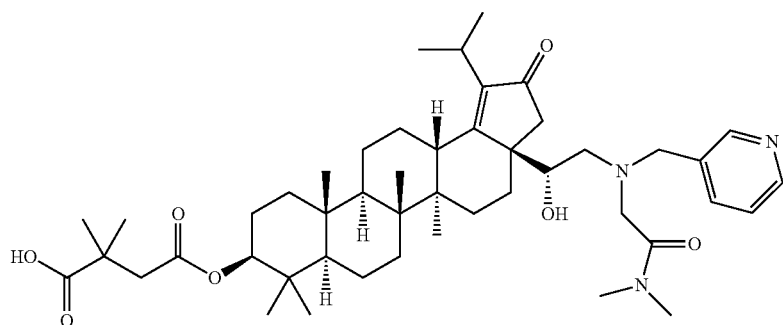
Example 355

Compound 424

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)-2-oxoethyl)(pyridin-3-
ylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

10



424

LC/MS: m/z calculated 789.5. found 790.5 (M+1)⁺

35

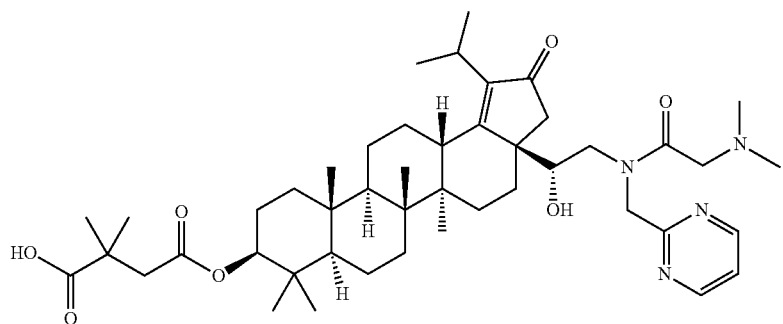
Example 356

Compound 425

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-(dimethylamino)-N-(pyrimidin-2-ylm-
ethyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

45



425

LC/MS: m/z calculated 790.5. found 791.5 (M+1)⁺

469

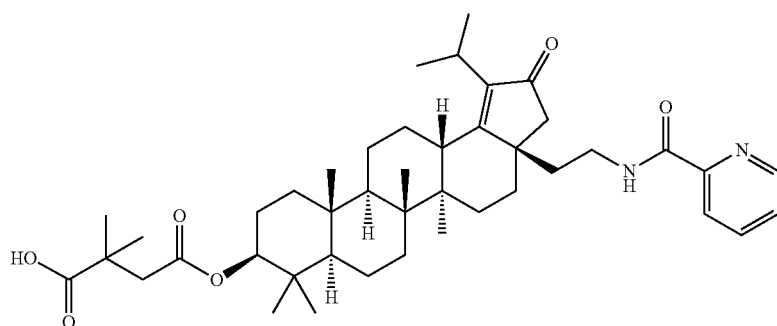
Example 357

470

Compound 426

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-(pi-
colinamido)ethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



426

LC/MS: m/z calculated 702.5. found 703.4 (M+1)⁺

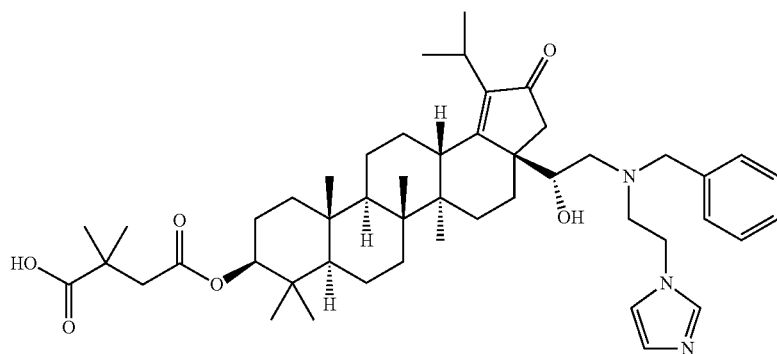
Example 358

35

Compound 427

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(1H-imidazol-1-yl)ethyl)(benzyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



427

LC/MS: m/z calculated 797.5. found 798.5 (M+1)⁺

471

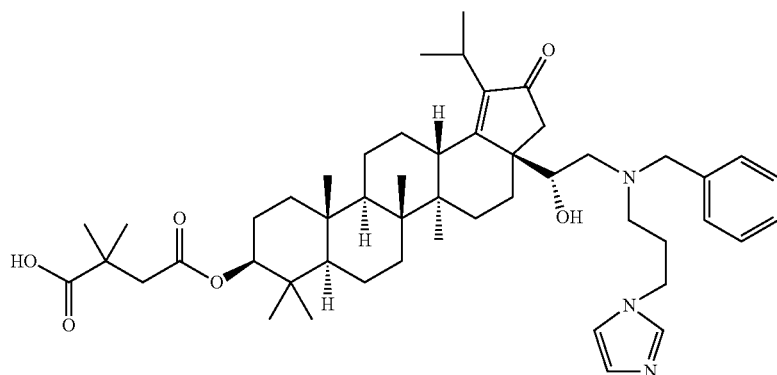
Example 359

472

Compound 428

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((3-(1H-imidazol-1-yl)propyl)(benzyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



428

LC/MS: m/z calculated 811.5. found 812.5 (M+1)⁺

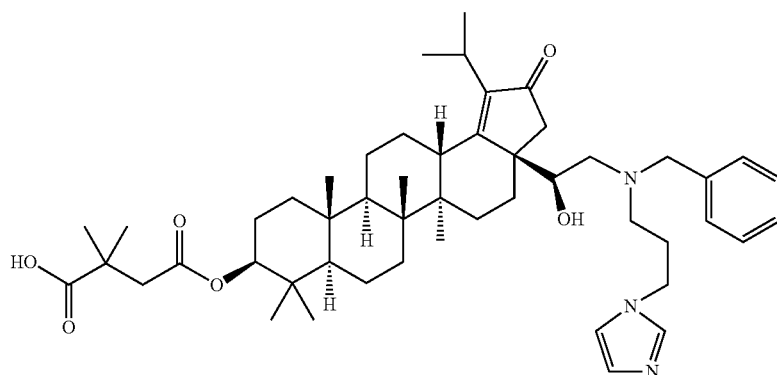
Example 360

35

Compound 429

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-((3-(1H-imidazol-1-yl)propyl)(benzyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



429

LC/MS: m/z calculated 811.5. found 812.5 (M+1)⁺

473

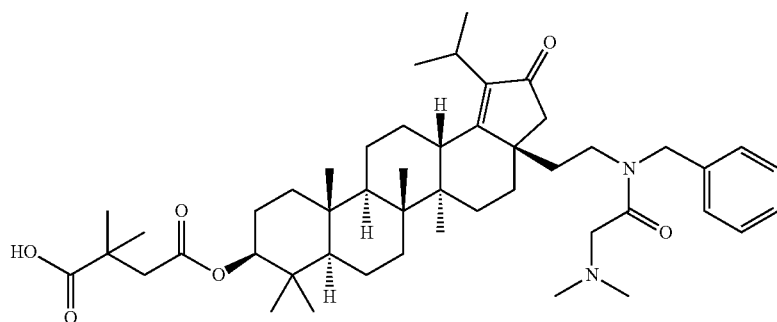
Example 361

474

Compound 430

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(N-benzyl-2-(dimethylamino)acetamido)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



430

LC/MS: m/z calculated 772.5. found 773.5 (M+1)⁺

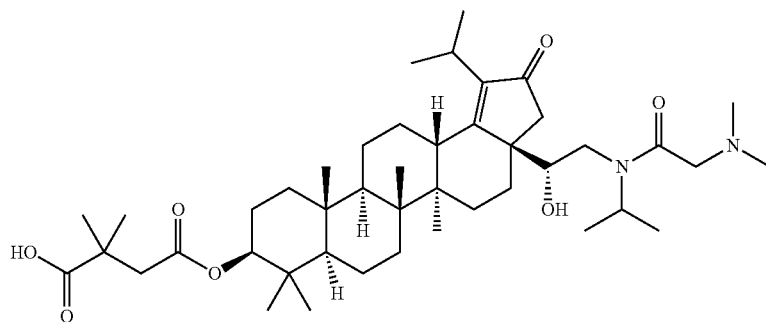
Example 362

35

Compound 431

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-(dimethylamino)-N-isopropylacetamido)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



431

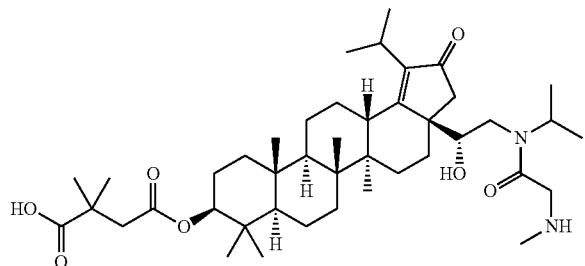
LC/MS: m/z calculated 740.5. found 741.5 (M+1)⁺

475

Example 363

Compound 432

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-isopropyl-2-(methylamino)
acetamido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



432

5

10

15

20

25

30

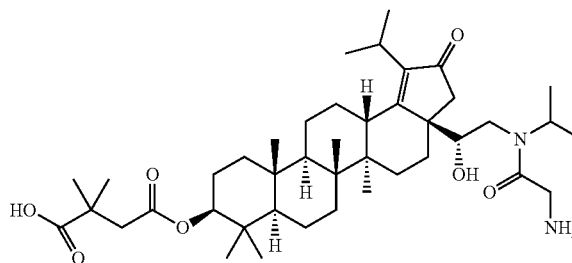
476

Example 364

Compound 433

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(2-amino-N-isopropylacetamido)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

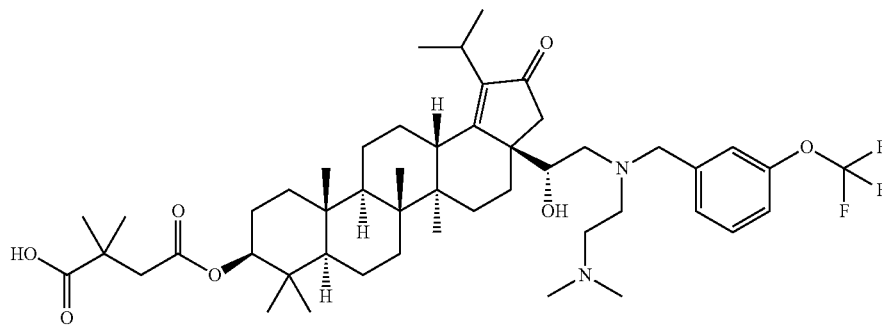
433

LC/MS: m/z calculated 712.5. found 713.5 (M+1)⁺

Example 365

Compound 434

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(3-(trifluoro-
methoxy)benzyl)amino)-1-hydroxyethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

LC/MS: m/z calculated 726.5. found 727.5 (M+1)⁺

434

LC/MS: m/z calculated 858.5. found 859.5 (M+1)⁺

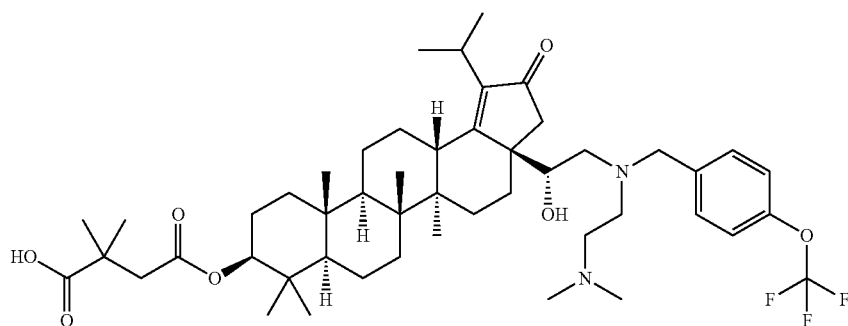
477

Example 366

478

Compound 435

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(4-(trifluo-
romethoxy)benzyl)amino)-1-hydroxyethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid 5 10



435

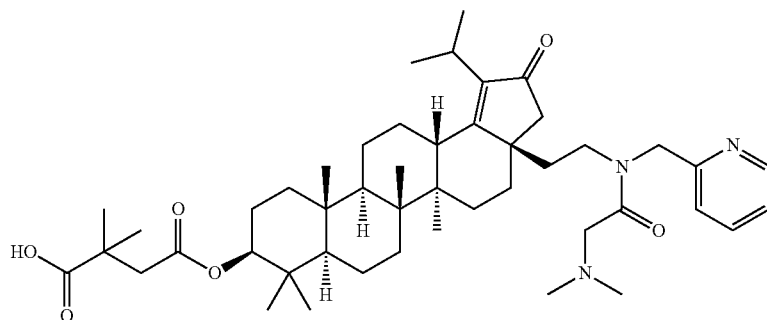
LC/MS: m/z calculated 858.5. found 859.5 (M+1)⁺

Example 367

Compound 436

35

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(2-(dimethylamino)-N-(pyridin-2-ylmethyl)aceta-
mido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid 40



436

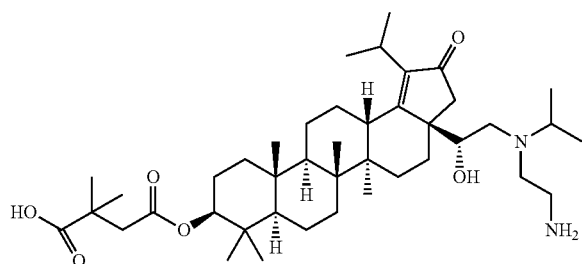
LC/MS: m/z calculated 773.5. found 774.5 (M+1)⁺

479

Example 368

Compound 437

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-aminoethyl)(isopropyl)amino)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



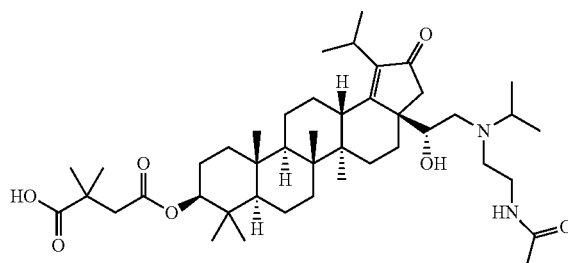
LC/MS: m/z calculated 698.5. found 699.5 (M+1)⁺

480

Example 369

Compound 438

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-acetamidoethyl)(isopropyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

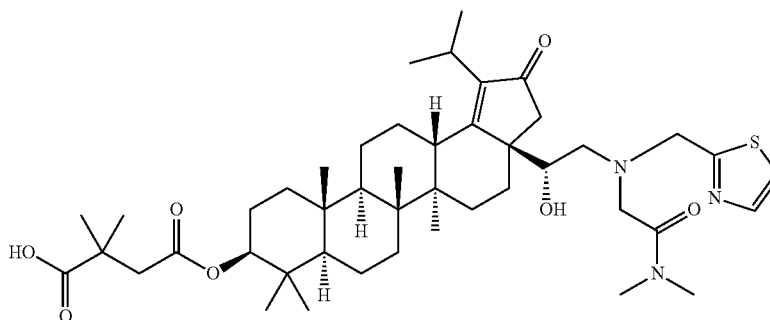


LC/MS: m/z calculated 740.5. found 741.5 (M+1)⁺

Example 370

Compound 439

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)-2-oxoethyl)(thiazol-2-
ylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid



LC/MS: m/z calculated 795.5. found 796.4 (M+1)⁺

481

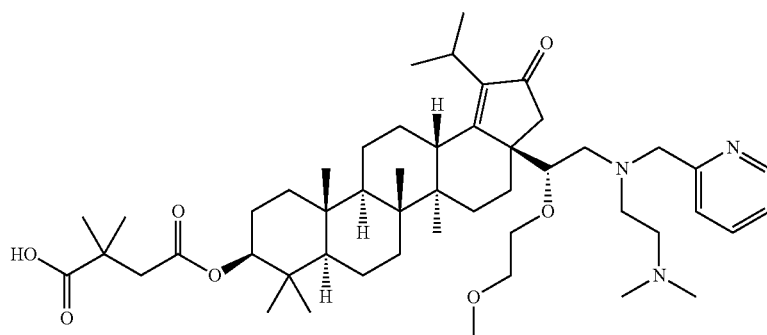
Example 371

482

Compound 440

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3a-((R)-2-methyl-5-(pyridin-2-ylmethyl)-8,11-dioxo-2,5-diazadodecan-7-yl)-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



440

LC/MS: m/z calculated 833.6. found 834.5 (M+1)⁺

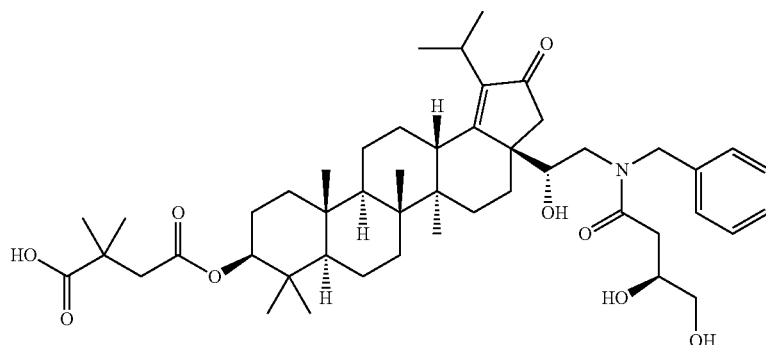
Example 372

35

Compound 441

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((S)-N-benzyl-3,4-dihydroxybutanamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



441

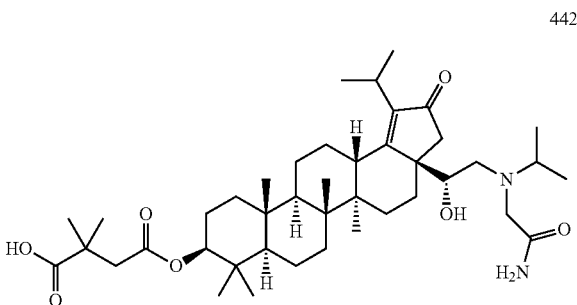
LC/MS: m/z calculated 805.5. found 806.5 (M+1)⁺

483

Example 373

Compound 442

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-amino-2-oxoethyl)(isopropyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

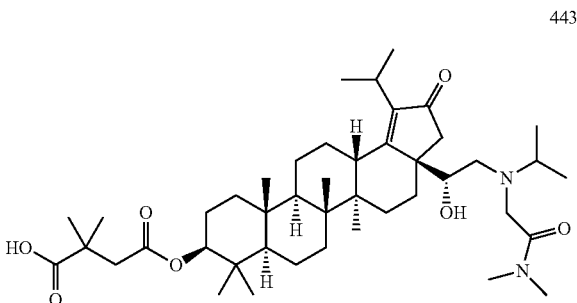


LC/MS: m/z calculated 712.5. found 713.5 (M+1)⁺

Example 374

Compound 443

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)-2-oxoethyl)(isopropyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



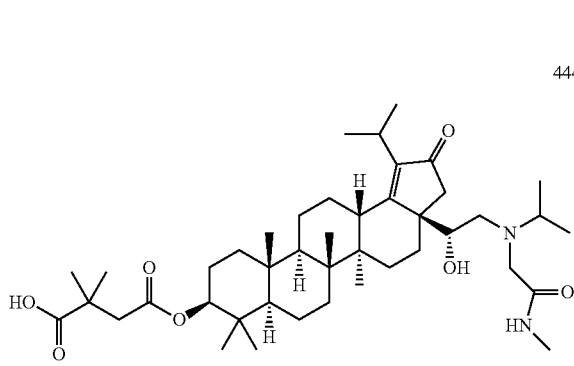
LC/MS: m/z calculated 740.5. found 741.5 (M+1)⁺

484

Example 375

Compound 444

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(isopropyl(2-(methylamino)-2-
oxoethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

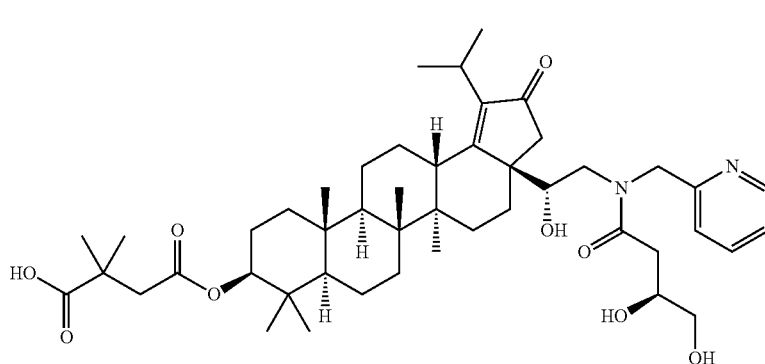


LC/MS: m/z calculated 726.5. found 727.5 (M+1)⁺

Example 376

Compound 445

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((S)-3,4-dihydroxy-N-(pyridin-2-ylmethyl)
butanamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid



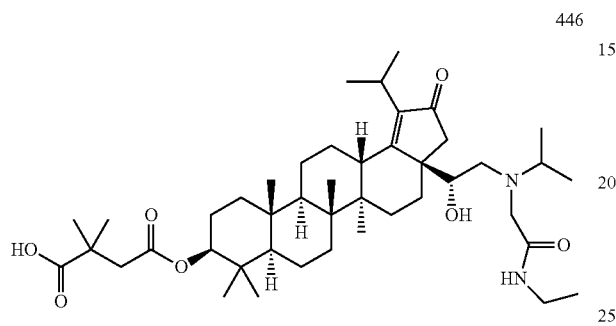
LC/MS: m/z calculated 806.5. found 807.5 (M+1)⁺

485

Example 377

Compound 446

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(ethylamino)-2-oxoethyl)(isopropyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

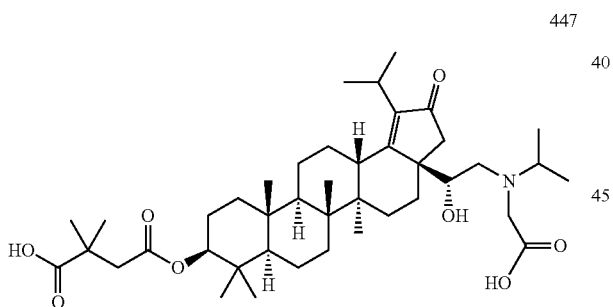


LC/MS: m/z calculated 740.5. found 741.5 (M+1)⁺

Example 378

Compound 447

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((carboxymethyl)(isopropyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 713.5. found 714.5 (M+1)⁺

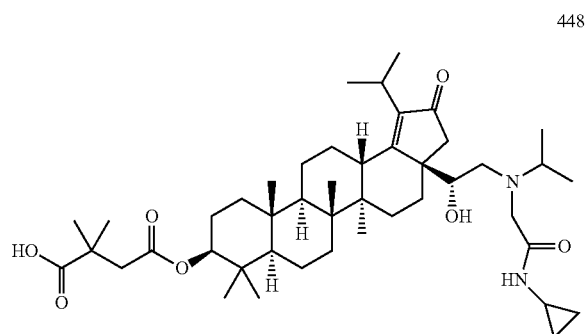
486

Example 379

Compound 448

5 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(cyclopropylamino)-2-oxoethyl)(isopro-
pyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

10

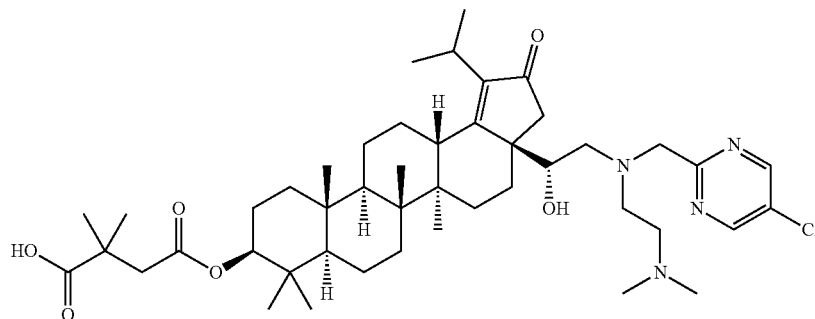


LC/MS: m/z calculated 752.5. found 753.5 (M+1)⁺

Example 380

Compound 449

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(((5-chloropyrimidin-2-yl)methyl)(2-(dim-
ethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopro-
pyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,
6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid



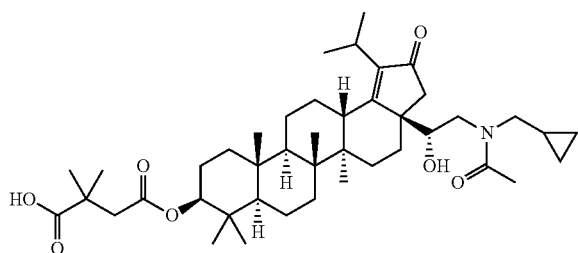
LC/MS: m/z calculated 810.5. found 811.5 (M+1)⁺

487

Example 381

Compound 450

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(cyclopropylmethyl)acetamido)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

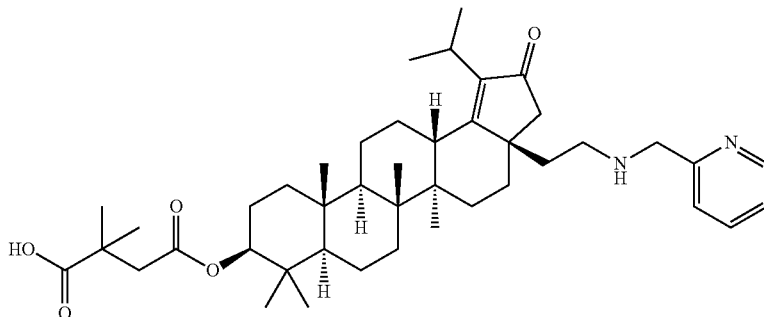


LC/MS: m/z calculated 709.5. found 710.5 (M+1)⁺

Example 382

Compound 451

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((py-
ridin-2-ylmethyl)amino)ethyl)-3,3a,4,5,5a,5b,6,7,7a,
8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid



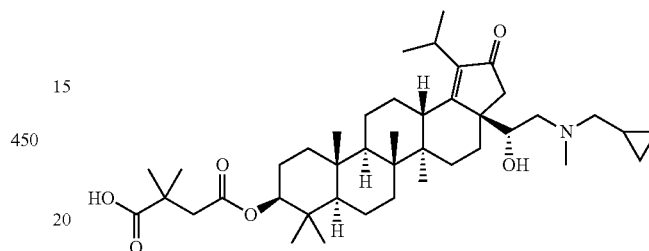
LC/MS: m/z calculated 688.5. found 689.5 (M+1)⁺

488

Example 383

Compound 452

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((cyclopropylmethyl)(methyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

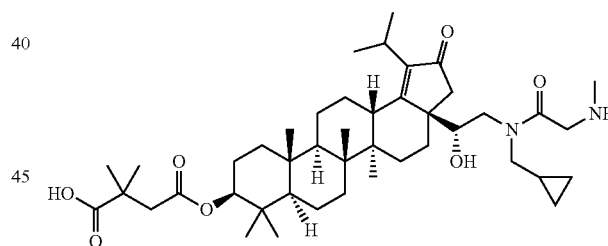


LC/MS: m/z calculated 681.5. found 682.5 (M+1)⁺

Example 384

Compound 453

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(cyclopropylmethyl)-2-(methylamino)
acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid



LC/MS: m/z calculated 738.5. found 739.5 (M+1)⁺

451

489

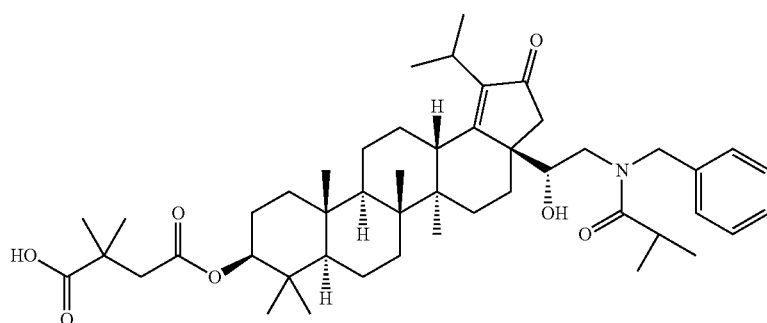
Example 385

490

Compound 454

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-benzylisobutyramido)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



454

LC/MS: m/z calculated 773.5. found 774.5 (M+1)⁺

35

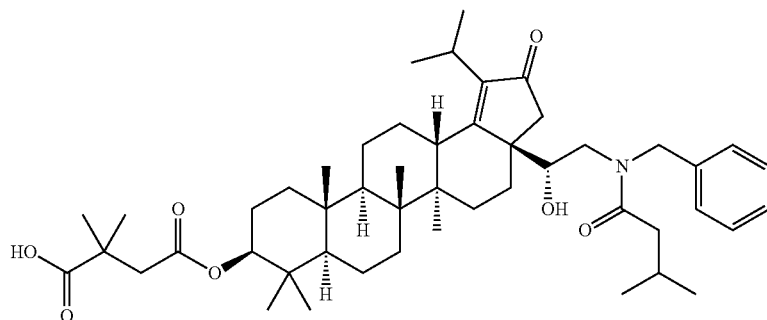
Example 386

Compound 455

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-benzyl-3-methylbutanamido)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



455

LC/MS: m/z calculated 787.5. found 788.5 (M+1)⁺

491

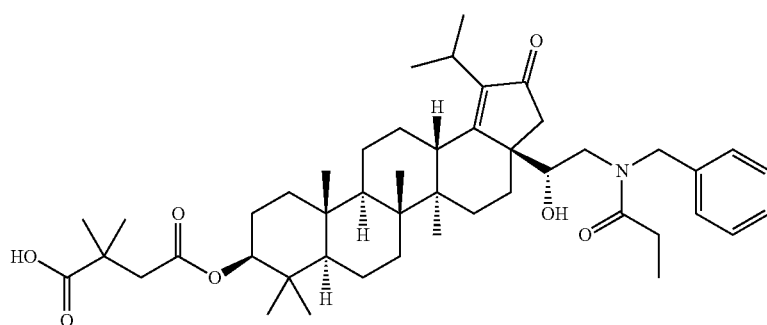
Example 387

492

Compound 456

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-benzylpropionamido)-1-hydroxyethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



456

LC/MS: m/z calculated 759.5. found 760.5 (M+1)⁺

35

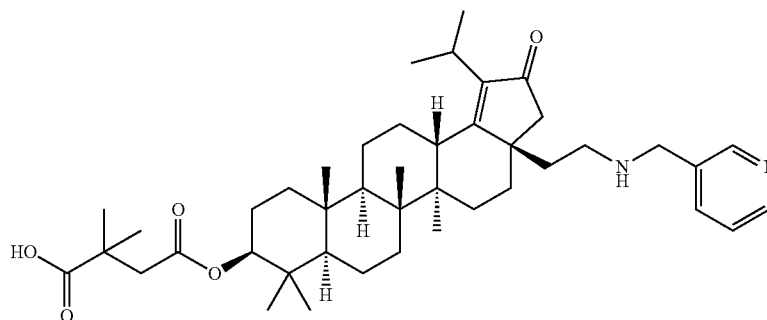
Example 388

Compound 457

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((py-
ridin-3-ylmethyl)amino)ethyl)-3,3a,4,5,5a,5b,6,7,7a,
8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

45



457

LC/MS: m/z calculated 688.5. found 689.5 (M+1)⁺

493

Example 389

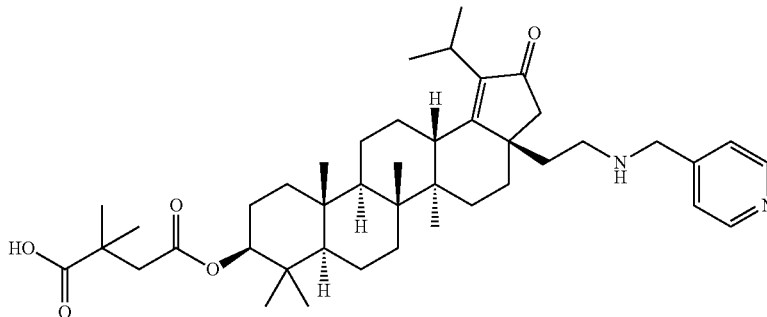
494

Compound 458

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((pyridin-4-ylmethyl)amino)ethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5

458



LC/MS: m/z calculated 688.5. found 689.5 (M+1)⁺

Example 390

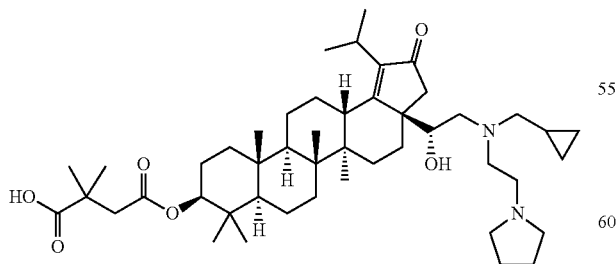
35

Compound 459

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((cyclopropylmethyl)(2-(pyrrolidin-1-yl)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45

50
459

60

65

LC/MS: m/z calculated 764.6. found 765.5 (M+1)⁺

495

Example 391

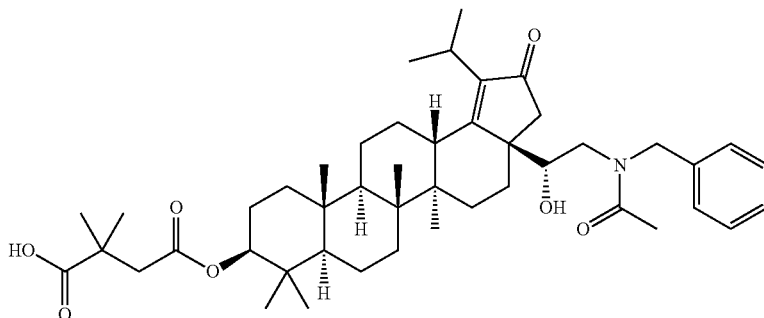
Compound 460

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-benzylacetamido)-1-hydroxyethyl)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5

496

460



LC/MS: m/z calculated 745.5. found 746.5 (M+1)⁺

Example 393

Example 392

35

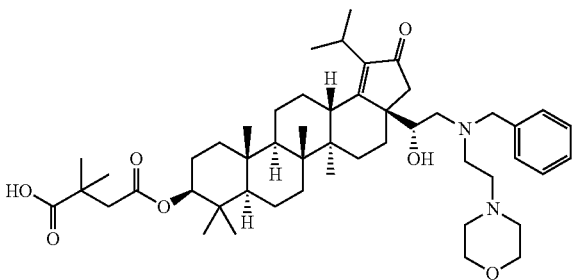
Compound 461

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(benzyl(2-morpholinoethyl)amino)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45

461 50



55

60

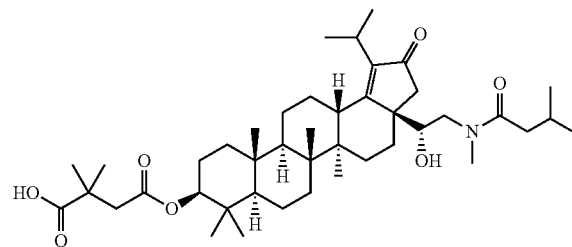
65

LC/MS: m/z calculated 816.6. found 817.5 (M+1)⁺

Compound 462

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N,3-dimethylbutanamido)-1-hydroxyethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

462



LC/MS: m/z calculated 711.5. found 712.5 (M+1)⁺

497

Example 394

Compound 463

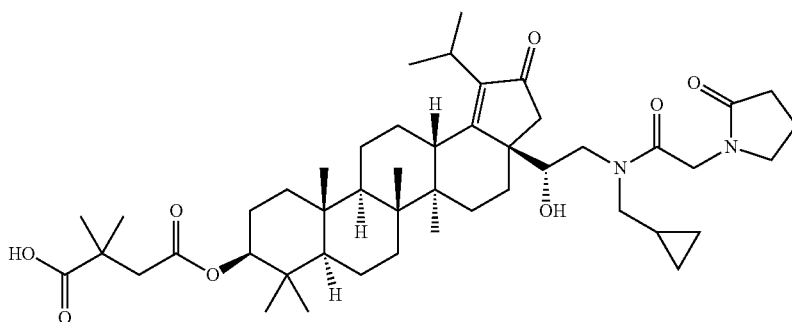
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(cyclopropylmethyl)-2-(2-oxopyrrolidin-
1-yl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

10

498

463

LC/MS: m/z calculated 792.5. found 793.5 (M+1)⁺

35

Example 396

Example 395

Compound 465

Compound 464

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-(isobutyryloxy)-2-(methylamino)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

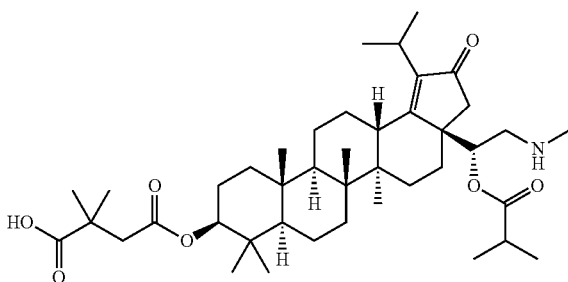
40

45

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((cyclobutylmethyl)amino)ethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

464 50

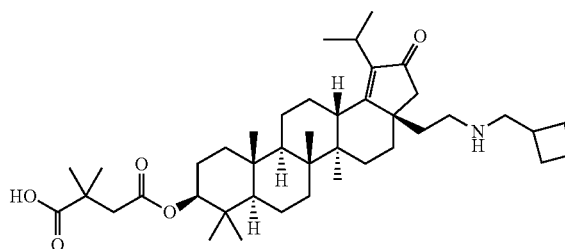
465



55

60

65

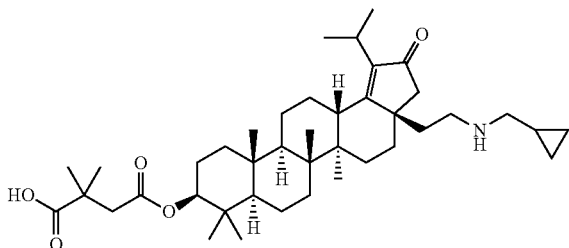
LC/MS: m/z calculated 697.5. found 698.5 (M+1)⁺LC/MS: m/z calculated 665.5. found 666.5 (M+1)⁺

499

Example 397

Compound 466

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((cyclopropylmethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

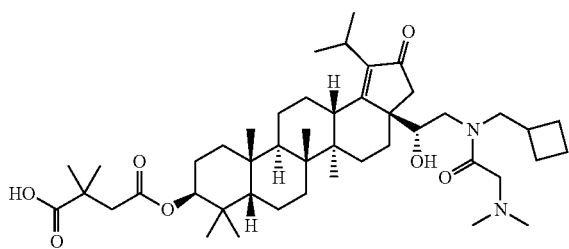


LC/MS: m/z calculated 651.5. found 652.5 (M+1)⁺

Example 398

Compound 467

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(N-(cyclobutylmethyl)-2-(dimethylamino)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



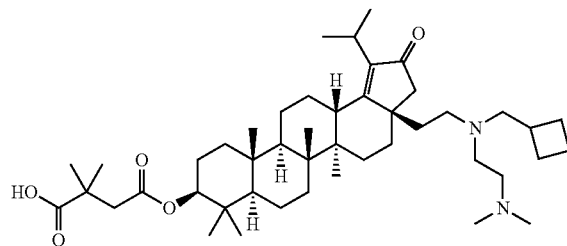
LC/MS: m/z calculated 766.5. found 767.5 (M+1)⁺

500

Example 399

Compound 468

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((cyclobutylmethyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

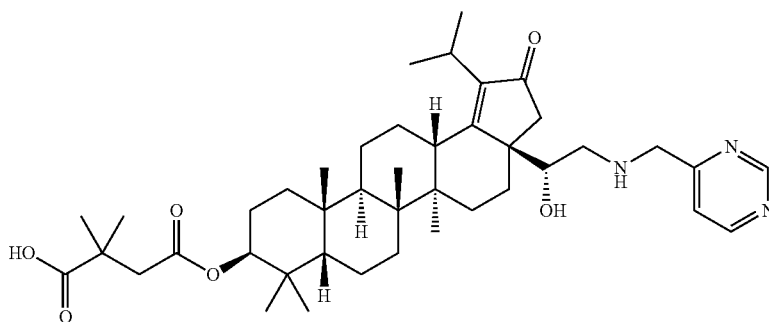


LC/MS: m/z calculated 736.6. found 737.5 (M+1)⁺

Example 400

Compound 469

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-hydroxy-2-((pyrimidin-4-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



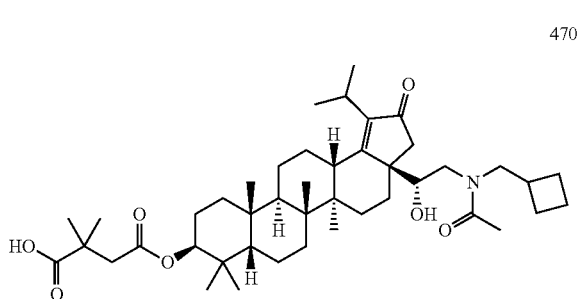
LC/MS: m/z calculated 705.5. found 706.5 (M+1)⁺

501

Example 401

Compound 470

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(N-(cyclobutylmethyl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

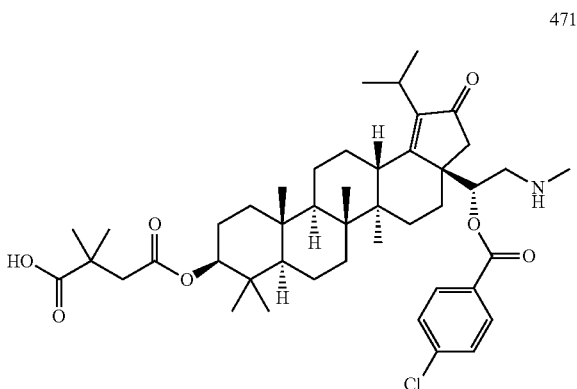


LC/MS: m/z calculated 723.5. found 724.5 (M+1)⁺

Example 402

Compound 471

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-((4-chlorobenzoyl)oxy)-2-(methylamino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



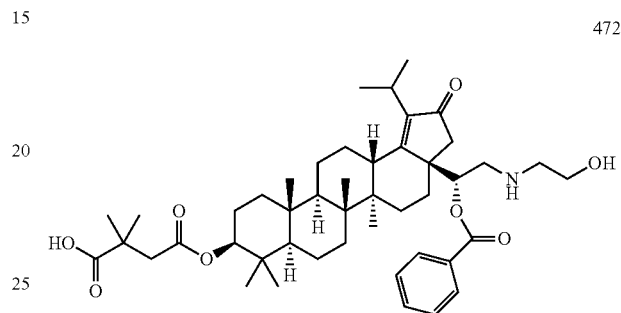
LC/MS: m/z calculated 765.4. found 766.4 (M+1)⁺

502

Example 403

Compound 472

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-(benzyloxy)-2-((2-hydroxyethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

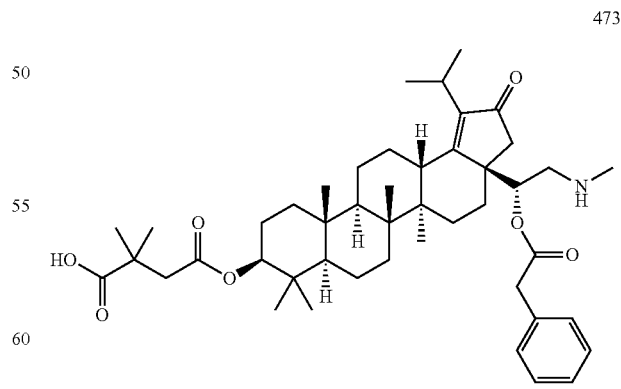


LC/MS: m/z calculated 761.5. found 762.4 (M+1)⁺

Example 404

Compound 473

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-3a-((R)-2-(methylamino)-1-(2-phenylacetoxy)ethyl)-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 745.5. found 746.5 (M+1)⁺

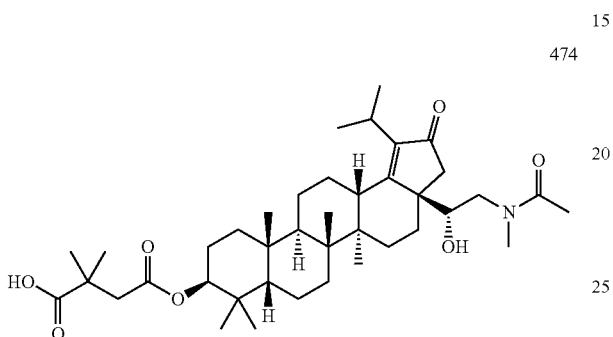
503

504

Example 405

Compound 474

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-methylacetamido) ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

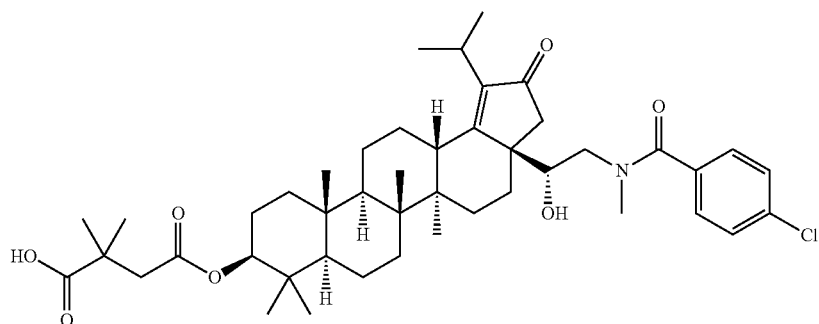


LC/MS: m/z calculated 669.5. found 670.4 (M+1)⁺

Example 406

Compound 475

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(4-chloro-N-methylbenzamido)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 765.4. found 766.4 (M+1)⁺

505

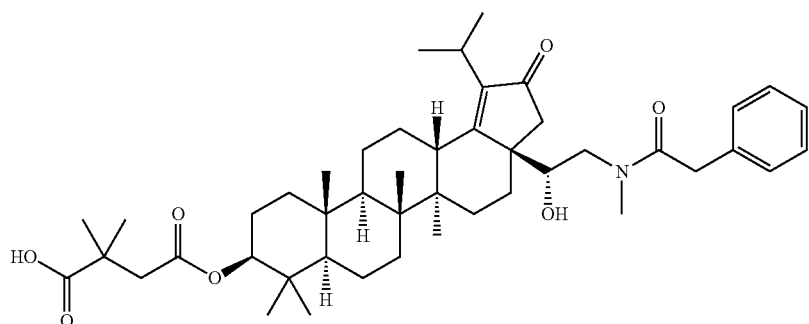
Example 407

506

Compound 476

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-methyl-2-phenylacetamido)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



476

LC/MS: m/z calculated 745.5. found 746.5 (M+1)⁺

35

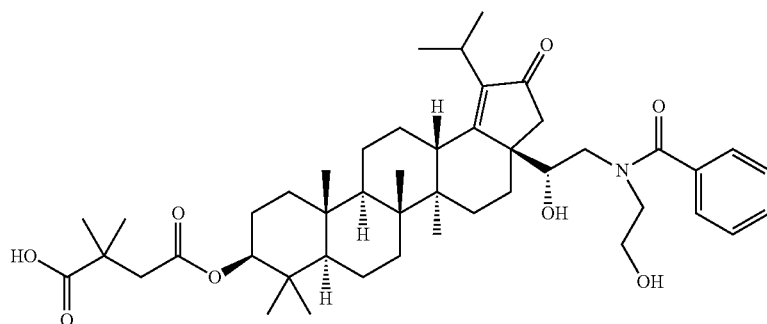
Example 408

Compound 477

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-(2-hydroxyethyl)benzamido)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



477

LC/MS: m/z calculated 761.5. found 762.4 (M+1)⁺

507

Example 409

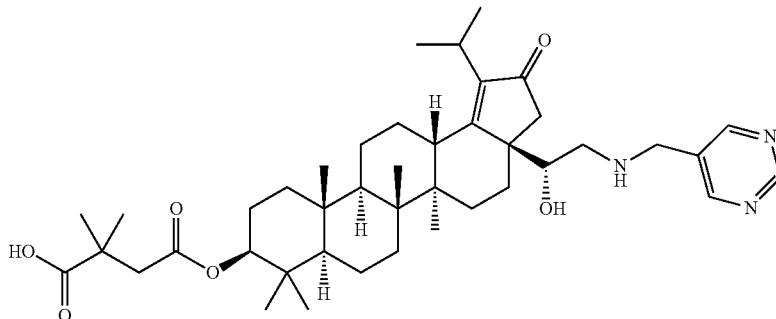
508

Compound 478

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((pyrimidin-5-ylmethyl)amino)
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5

478



30

LC/MS: m/z calculated 705.5. found 706.5 (M+1)⁺

Example 410

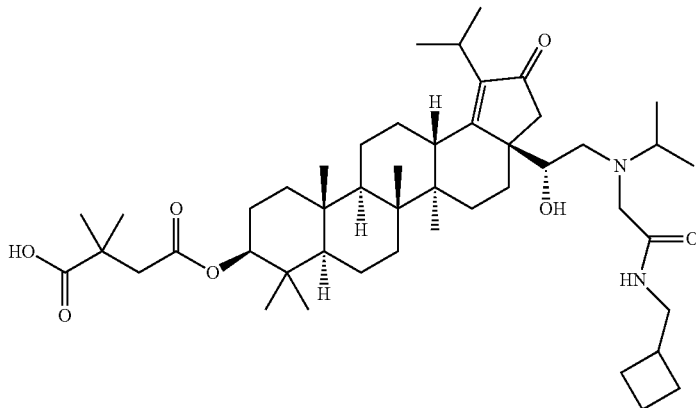
Compound 479

35

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-((cyclobutylmethyl)amino)-2-oxoethyl)
(isopropyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,
5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

479



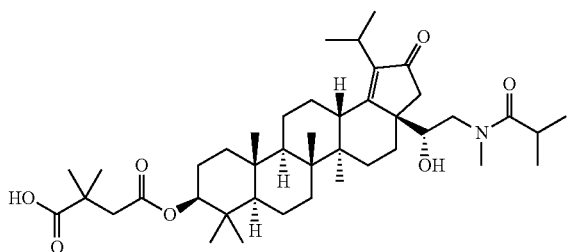
LC/MS: m/z calculated 780.6. found 781.6 (M+1)⁺

509

Example 411

Compound 480

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-methylisobutyramido)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid



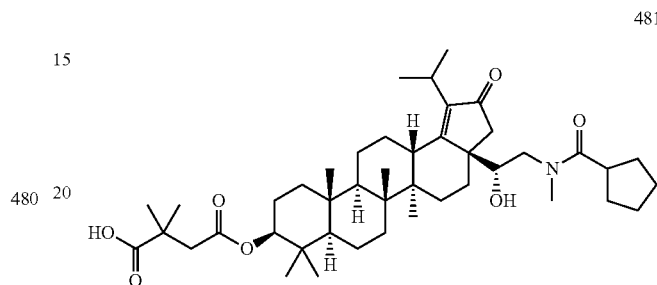
LC/MS: m/z calculated 697.5. found 698.5 (M+1)⁺

510

Example 412

Compound 481

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-methylcyclopentanecarboxa-
mido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

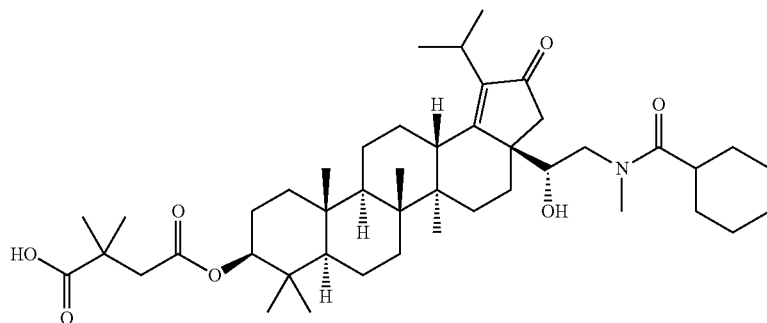


LC/MS: m/z calculated 723.5. found 724.5 (M+1)⁺

Example 413

Compound 482

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-methylcyclohexanecarboxa-
mido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid



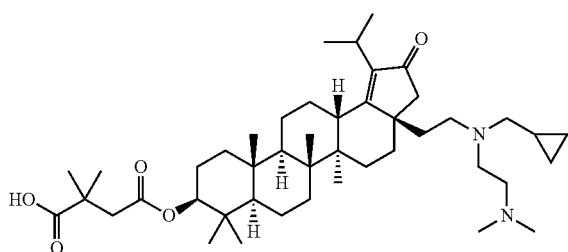
LC/MS: m/z calculated 737.5. found 738.5 (M+1)⁺

511

Example 414

Compound 483

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((cyclopropylmethyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



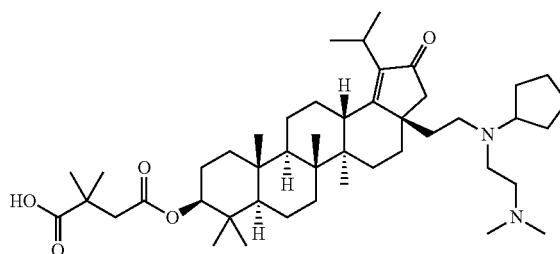
LC/MS: m/z calculated 722.6. found 723.6 (M+1)⁺

512

Example 415

Compound 484

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-(cyclopentyl(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

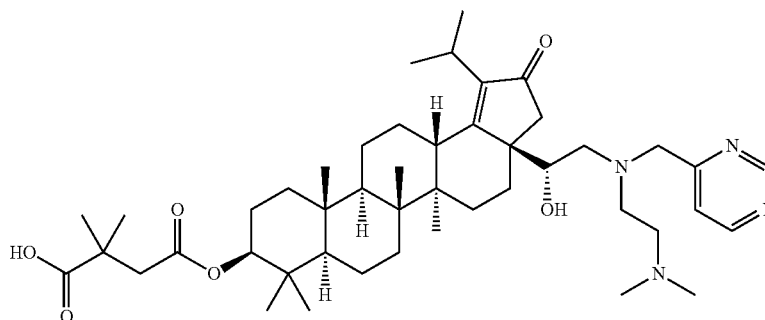


LC/MS: m/z calculated 736.6. found 737.5 (M+1)⁺

Example 416

Compound 485

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-(dimethylamino)ethyl)(pyrimidin-4-ylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 776.5. found 777.5 (M+1)⁺

513

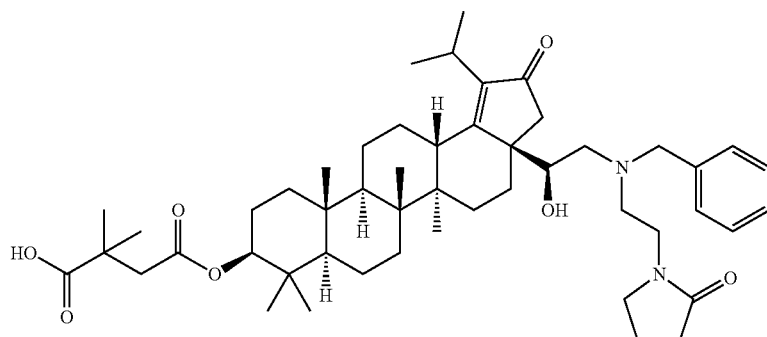
514

Example 417

Compound 486

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-
2-(benzyl(2-(2-oxopyrrolidin-1-yl)ethyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



486

LC/MS: m/z calculated 814.5. found 815.5 (M+1)⁺

35

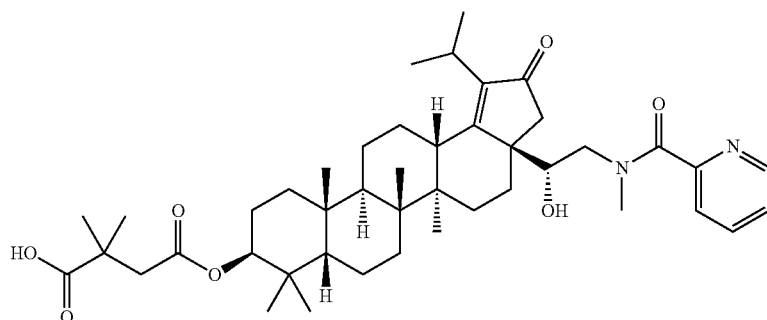
Example 418

Compound 487

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-methylpicolinamido)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



487

LC/MS: m/z calculated 732.5. found 733.5 (M+1)⁺

515

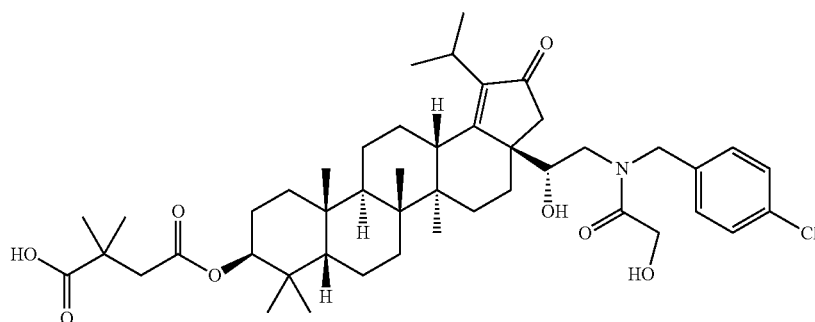
Example 419

516

Compound 488

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(4-chlorobenzyl)-2-hydroxyacetamido)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



488

LC/MS: m/z calculated 795.4. found 796.3 (M+1)⁺

35

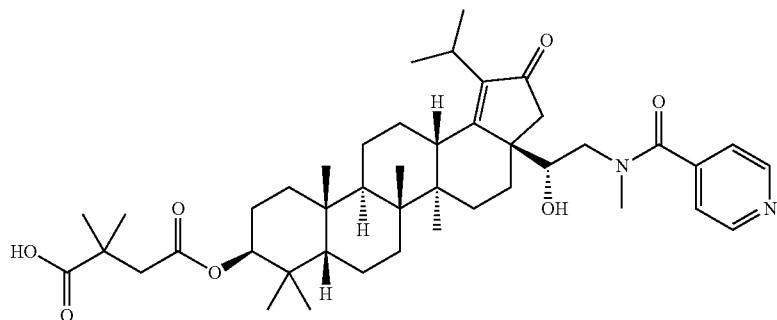
Example 420

Compound 489

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-methylisonicotinamido)ethyl)-
1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,
5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



489

LC/MS: m/z calculated 732.5. found 733.5 (M+1)⁺

517

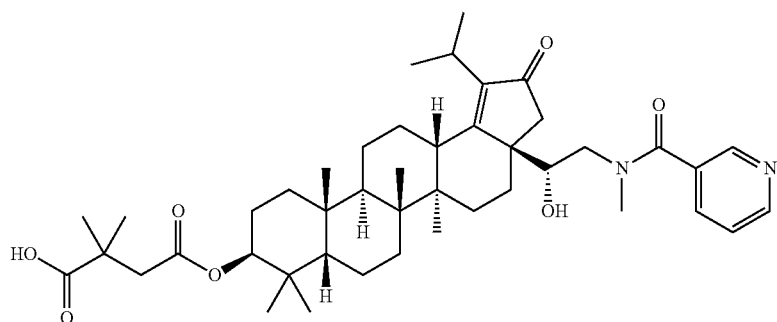
Example 421

518

Compound 490

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(N-methylnicotinamido) ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



490

LC/MS: m/z calculated 732.5. found 733.4 (M+1)⁺

35

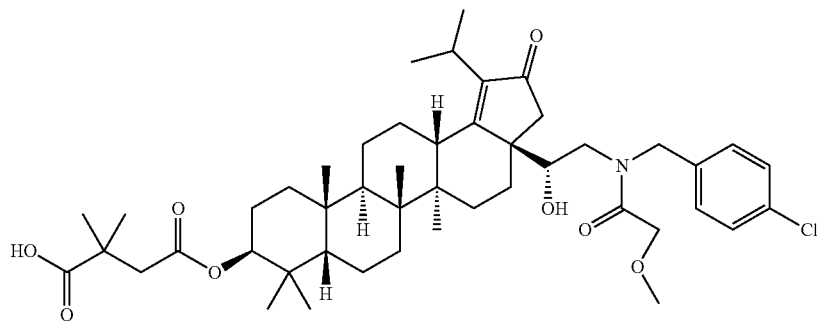
Example 422

Compound 491

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(4-chlorobenzyl)-2-methoxyacetamido)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



491

LC/MS: m/z calculated 809.5. found 810.3 (M+1)⁺

519

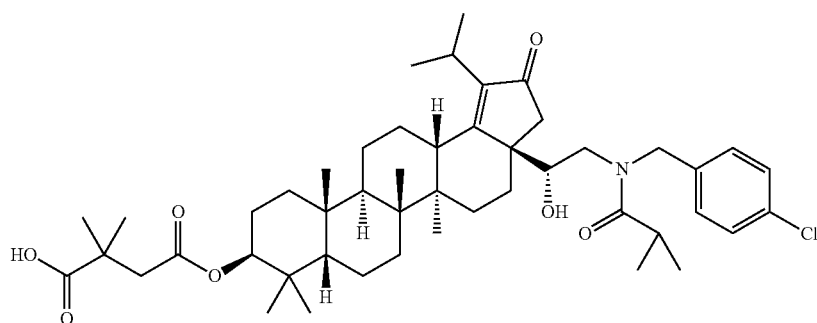
520

Example 423

Compound 492

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(4-chlorobenzyl)isobutyramido)-1-hy-
droxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

5



492

LC/MS: m/z calculated 807.5. found 808.5 (M+1)⁺

35

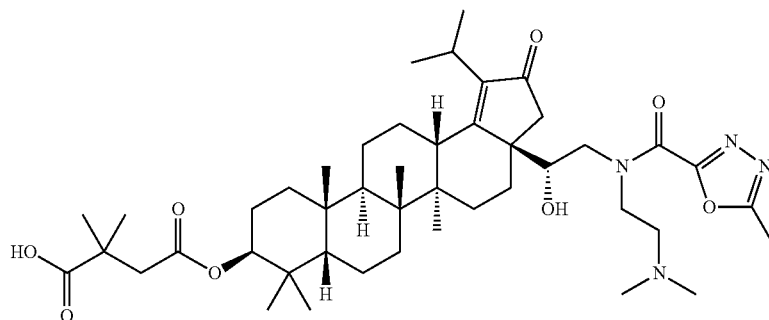
Example 424

Compound 493

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(2-(dimethylamino)ethyl)-5-methyl-1,3,4-
oxadiazole-2-carboxamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



493

LC/MS: m/z calculated 794.5. found 795.5 (M+1)⁺

521

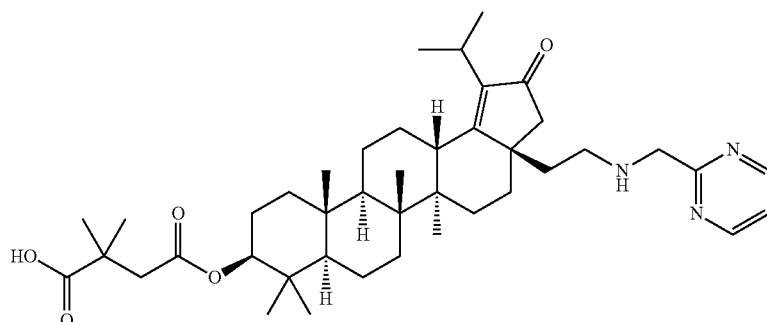
Example 425

522

Compound 494

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((pyrimidin-2-ylmethyl)amino)ethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



494

LC/MS: m/z calculated 689.5. found 690.4 (M+1)⁺

35

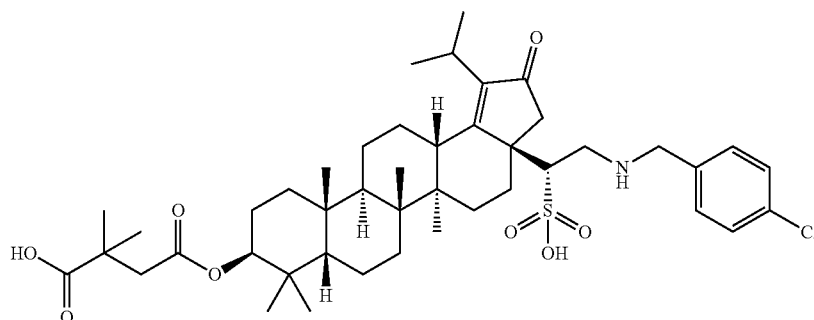
Example 427

Compound 496

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-sulfoethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



496

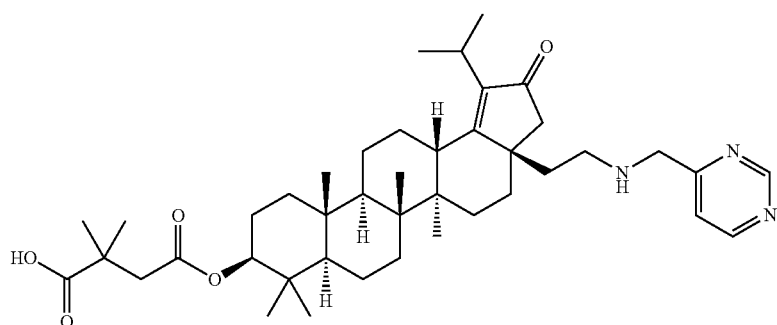
LC/MS: m/z calculated 801.4. found 802.2 (M+1)⁺

Example 428

Compound 497

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((pyrimidin-4-ylmethyl)amino)ethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



497

LC/MS: m/z calculated 689.5. found 690.4 (M+1)⁺

35

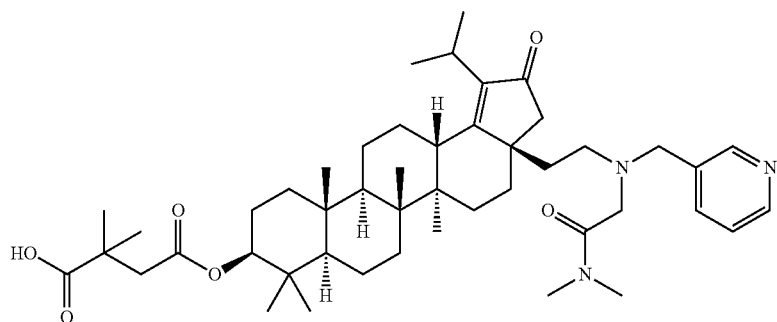
Example 429

Compound 498

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((2-(dimethylamino)-2-oxoethyl)(pyridin-3-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



498

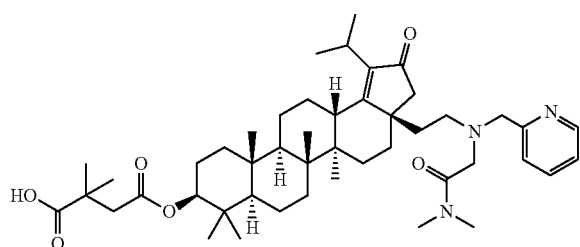
LC/MS: m/z calculated 773.5. found 774.5 (M+1)⁺

525

Example 430

Compound 499

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((2-(dimethylamino)-2-oxoethyl)(pyridin-2-ylm-
ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pen-
tamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,
11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

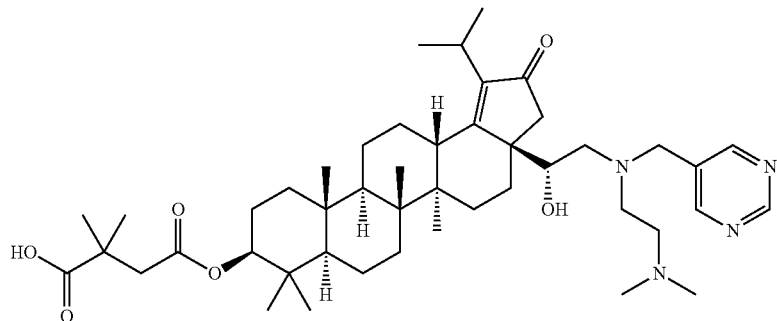


LC/MS: m/z calculated 773.5. found 774.5 (M+1)⁺

Example 431

Compound 500

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(pyrimidin-5-ylm-
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid



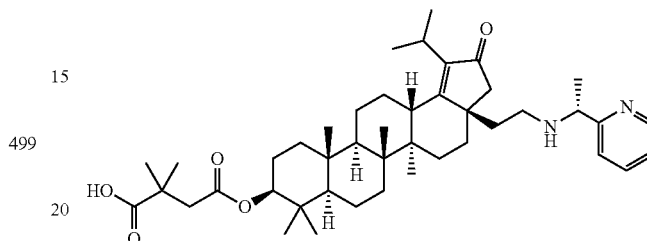
LC/MS: m/z calculated 776.5. found 777.4 (M+1)⁺

526

Example 433

Compound 502

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-
(((R)-1-(pyridin-2-yl)ethyl)amino)ethyl)-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

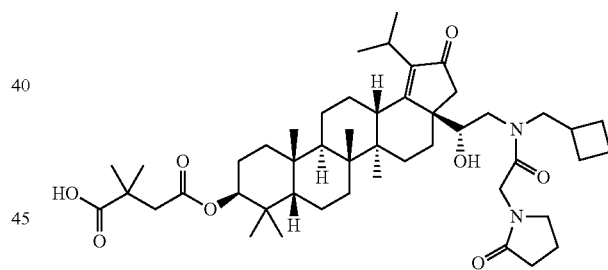


LC/MS: m/z calculated 702.5. found 703.3 (M+1)⁺

Example 434

Compound 503

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(cyclobutylmethyl)-2-(2-oxopyrrolidin-1-
yl)acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,
8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid



LC/MS: m/z calculated 806.5. found 806.9 (M+1)⁺

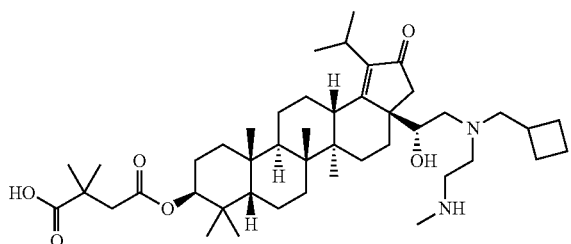
500

527

Example 435

Compound 504

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((cyclobutylmethyl)(2-(methylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

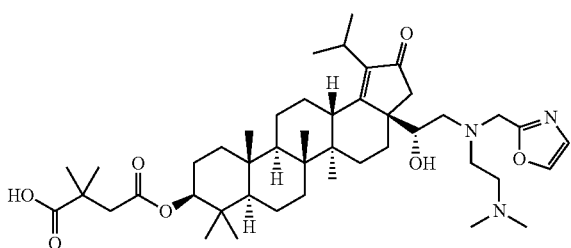


LC/MS: m/z calculated 738.5. found 739.5 (M+1)⁺

Example 436

Compound 505

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-(dimethylamino)ethyl)(oxazol-2-ylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

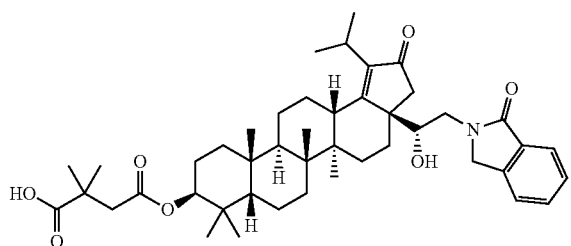


LC/MS: m/z calculated 765.5. found 765.9 (M+1)⁺

Example 437

Compound 506

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-hydroxy-2-(1-oxoisindolin-2-yl)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



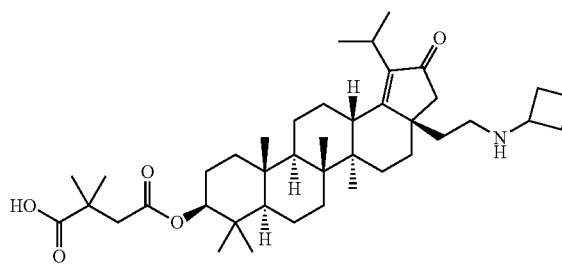
LC/MS: m/z calculated 729.5. found 729.9 (M+1)⁺

528

Example 438

Compound 507

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-(cyclobutylamino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

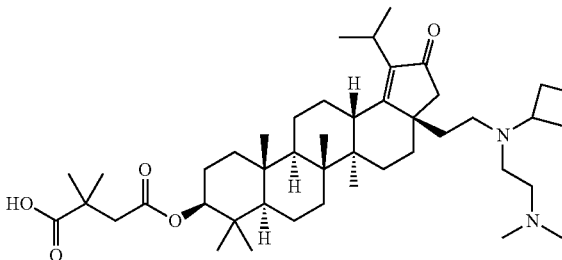


LC/MS: m/z calculated 651.5. found 652.0 (M+1)⁺

Example 439

Compound 508

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-(cyclobutyl(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

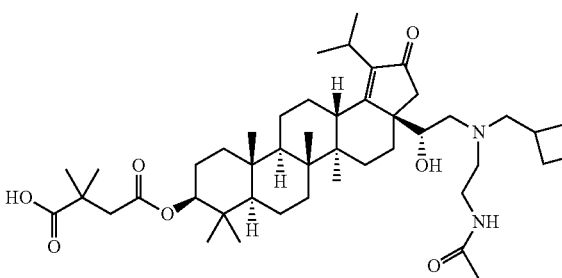


LC/MS: m/z calculated 722.6. found 723.0 (M+1)⁺

Example 440

Compound 509

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((2-(acetamidoethyl)(cyclobutylmethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 766.5. found 766.9 (M+1)⁺

529

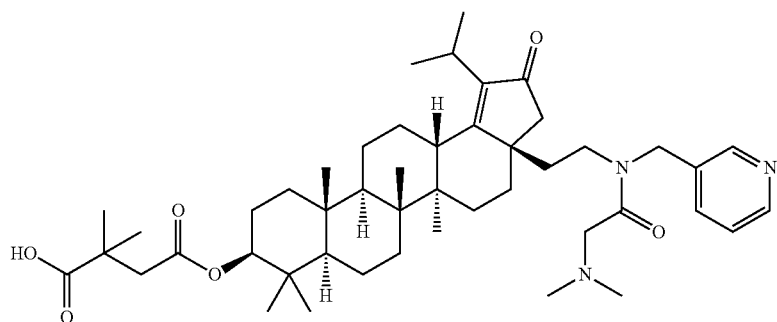
530

Example 441

Compound 510

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(2-(dimethylamino)-N-(pyridin-3-ylmethyl)aceta-
mido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
oxy)-2,2-dimethyl-4-oxobutanoic acid

5



510

LC/MS: m/z calculated 773.5. found 774.5 (M+1)⁺

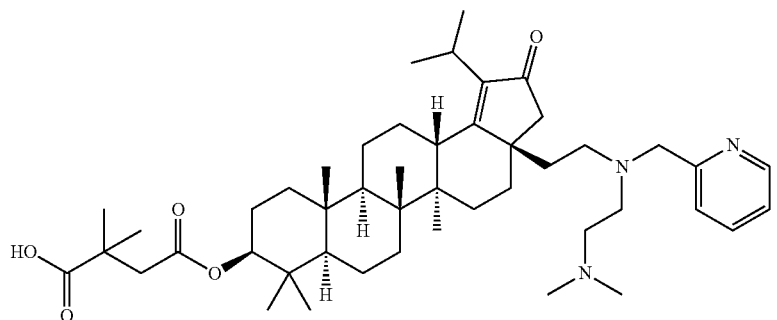
35

Example 442

Compound 511

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(2-(dimethylamino)ethyl)(pyridin-2-ylmethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



511

LC/MS: m/z calculated 759.6. found 760.5 (M+1)⁺

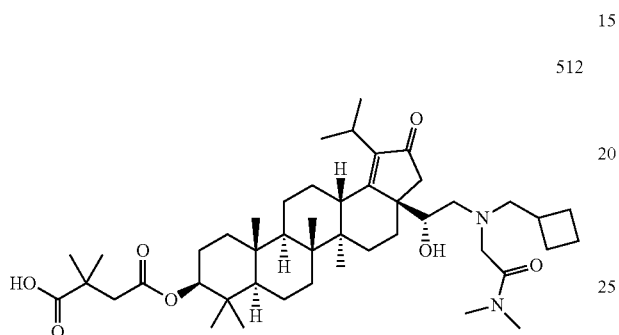
531

Example 443

532

Compound 512

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((cyclobutylmethyl)(2-(dimethylamino)-2-
 oxoethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,
 8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
 10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid

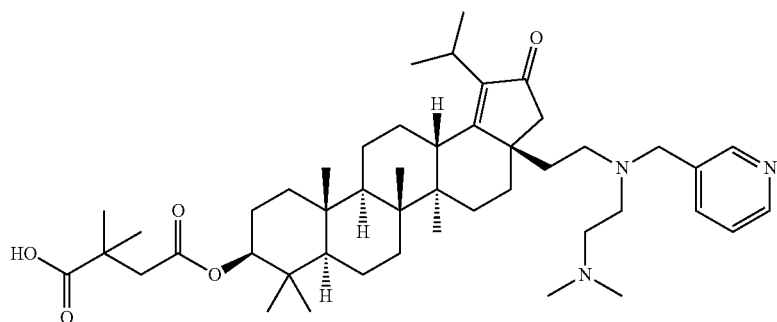


LC/MS: m/z calculated 766.5. found 767.5 (M+1)⁺

Example 444

Compound 513

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((2-(dimethylamino)ethyl)(pyridin-3-ylmethyl)
 amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 759.6. found 760.5 (M+1)⁺

533

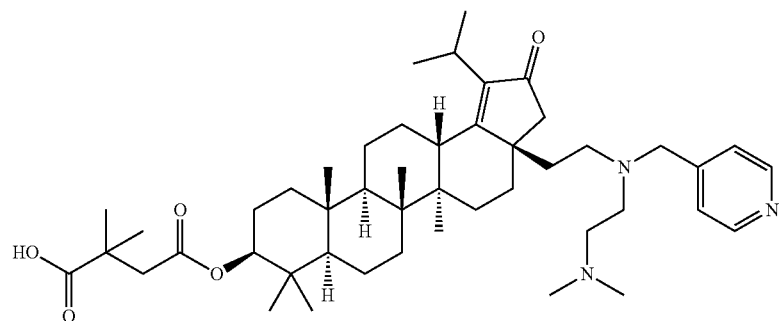
Example 445

534

Compound 514

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((2-(dimethylamino)ethyl)(pyridin-4-ylmethyl)
 amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentameth-
 yl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



514

LC/MS: m/z calculated 759.6. found 760.5 (M+1)⁺

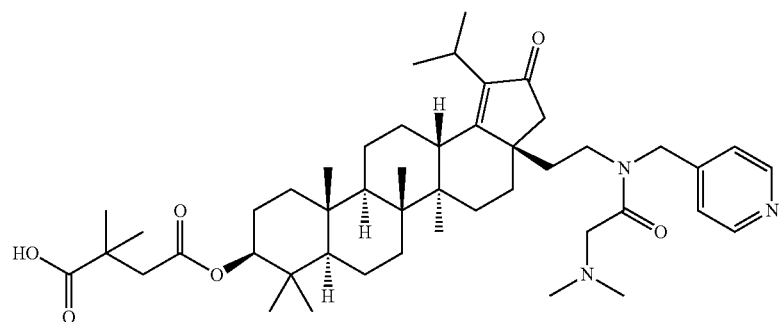
Example 446

Compound 515

40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 (2-(dimethylamino)-N-(pyridin-4-ylmethyl)aceta-
 mido)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-
 2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,
 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)
 oxy)-2,2-dimethyl-4-oxobutanoic acid

45



515

LC/MS: m/z calculated 773.5. found 774.5 (M+1)⁺

535

Example 447

536

Compound 516

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((cyclobutylmethyl)(2-(N-methylacetamido)
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

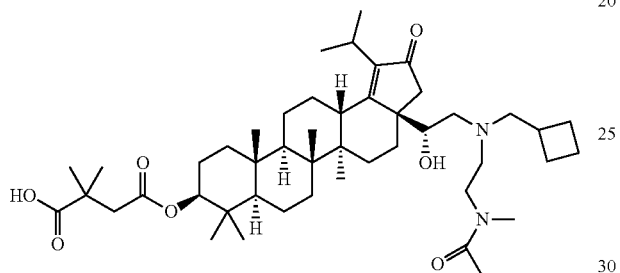
5

10

15

516

20



30

LC/MS: m/z calculated 780.6. found 781.4 (M+1)⁺

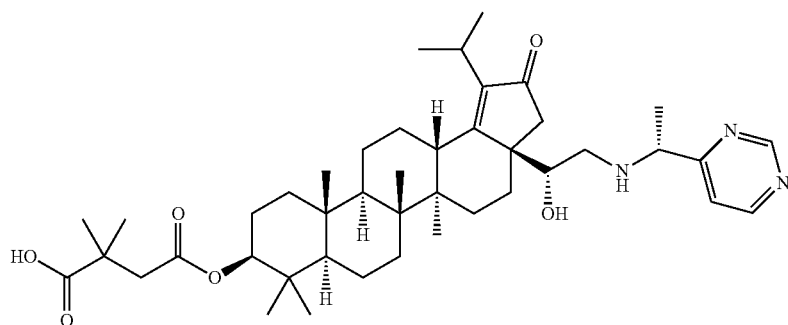
Example 448

Compound 517

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(((R)-1-(pyrimidin-4-yl)ethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

35

40



517

LC/MS: m/z calculated 719.5. found 720.4 (M+1)⁺

537

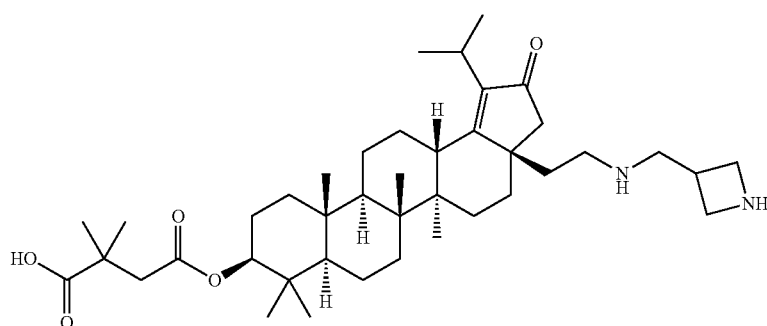
Example 449

538

Compound 518

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((azetidin-3-ylmethyl)amino)ethyl)-1-isopropyl-5a,
 5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
 8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid

5



518

LC/MS: m/z calculated 666.5. found 667.4 (M+1)⁺

35

Example 450

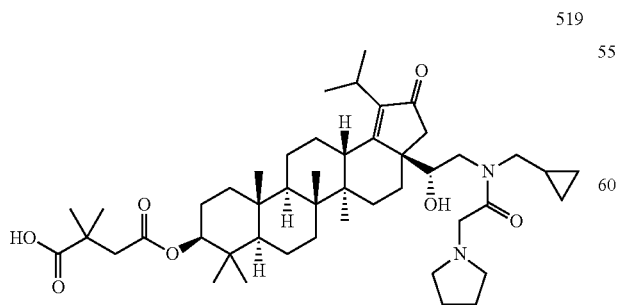
40

Compound 519

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(N-(cyclopropylmethyl)-2-(pyrrolidin-1-yl)
 acetamido)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid

45

50



519

55

60

65

LC/MS: m/z calculated 778.5. found 779.5 (M+1)⁺

539

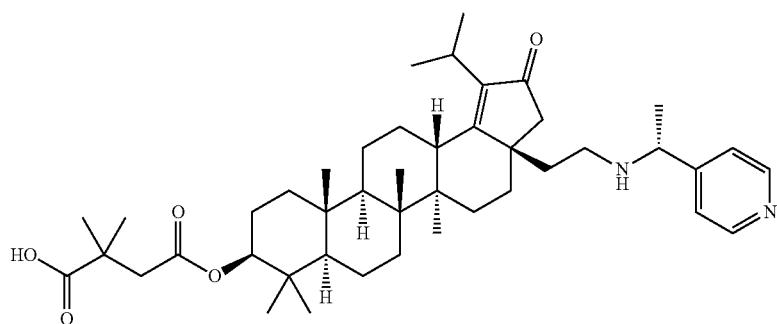
Example 451

540

Compound 520

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-(((R)-1-(pyridin-4-yl)ethyl)amino)ethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



520

LC/MS: m/z calculated 702.5. found 703.5 (M+1)⁺

35

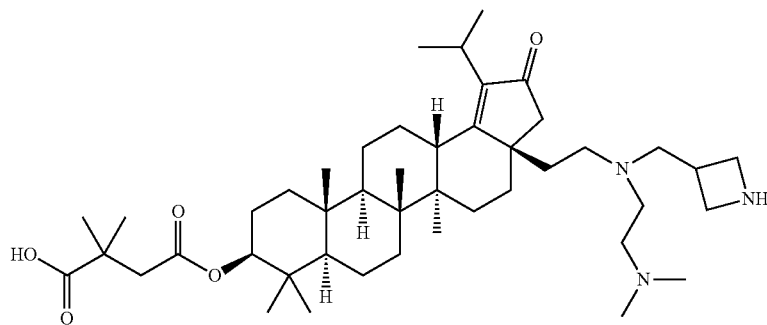
Example 452

Compound 521

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((azetidin-3-ylmethyl)(2-(dimethylamino)ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



521

LC/MS: m/z calculated 737.6. found 738.7 (M+1)⁺

541

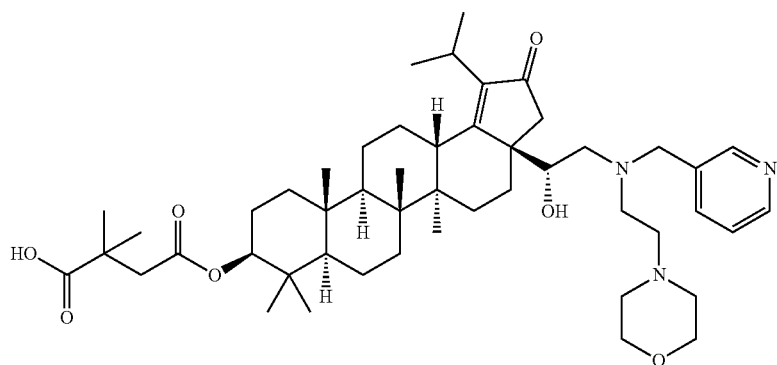
Example 454

542

Compound 523

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((2-morpholinoethyl)(pyridin-3-
 ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-
 pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
 11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
 chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



523

LC/MS: m/z calculated 817.6. found 818.5 (M+1)⁺

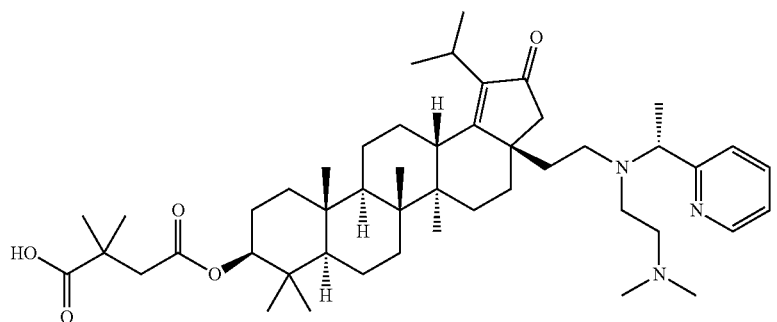
Example 455

Compound 524

40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((2-(dimethylamino)ethyl)((R)-1-(pyridin-2-yl)ethyl)
 amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

45



524

LC/MS: m/z calculated 773.6. found 774.5 (M+1)⁺

543

544

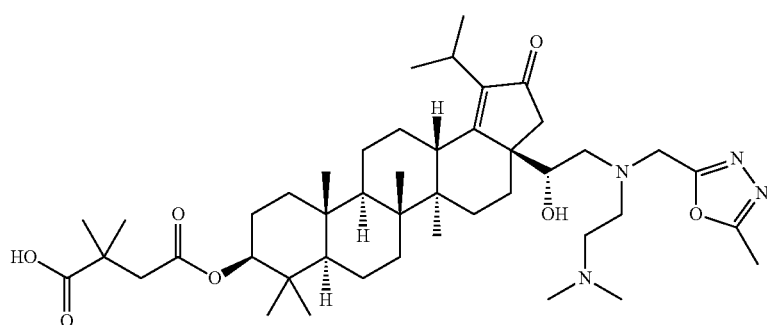
Example 456

Compound 525

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((2-(dimethylamino)ethyl)((5-methyl-1,3,4-
 oxadiazol-2-yl)methyl)amino)-1-hydroxyethyl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5

10



525

35

LC/MS: m/z calculated 780.6. found 781.5 (M+1)⁺

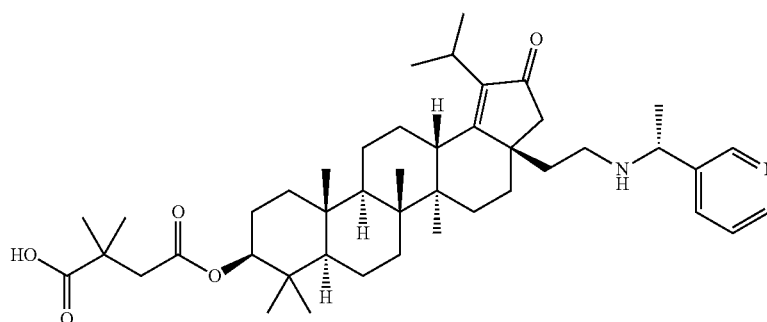
Example 457

Compound 526

40

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
 propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-
 (((R)-1-(pyridin-3-yl)ethyl)amino)ethyl)-3,3a,4,5,5a,
 5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

45



526

LC/MS: m/z calculated 702.5. found 703.5 (M+1)⁺

545

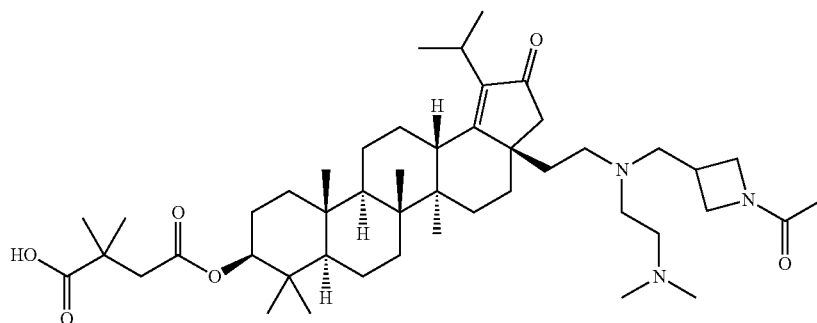
Example 458

546

Compound 527

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 (((1-acetylazetidin-3-yl)methyl)(2-(dimethylamino)
 ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pen-
 tamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,
 11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
 chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



527

LC/MS: m/z calculated 779.6. found 780.7 (M+1)⁺

35

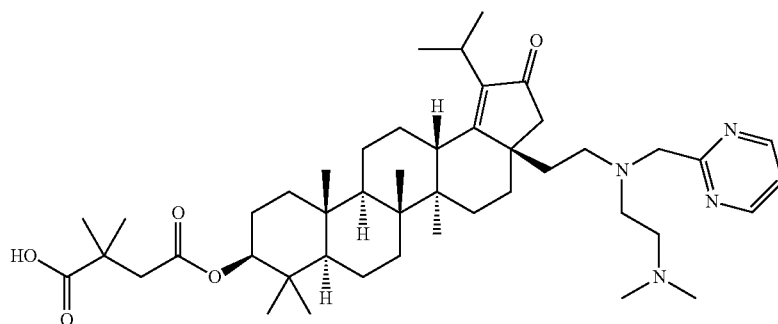
Example 459

Compound 528

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((2-(dimethylamino)ethyl)(pyrimidin-2-ylmethyl)
 amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



528

LC/MS: m/z calculated 760.5. found 761.7 (M+1)⁺

547

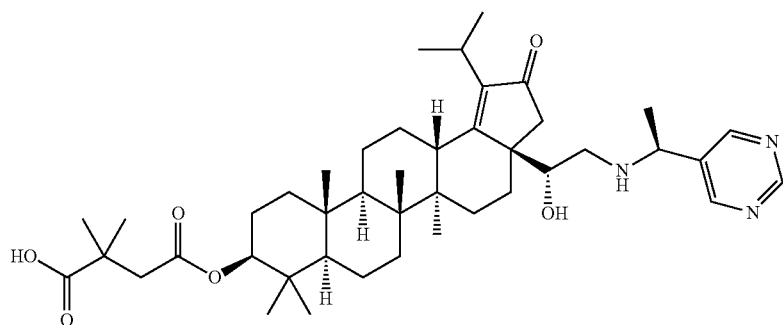
548

Example 460

Compound 529

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(((S)-1-(pyrimidin-5-yl)ethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



529

LC/MS: m/z calculated 719.5. found 720.5 (M+1)⁺

35

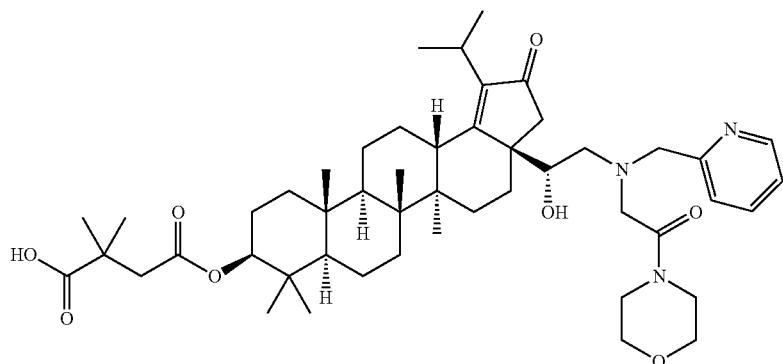
Example 461

Compound 530

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-((2-morpholino-2-oxoethyl)(pyri-
din-2-ylmethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

40

45



530

LC/MS: m/z calculated 831.5. found 832.7 (M+1)⁺

549

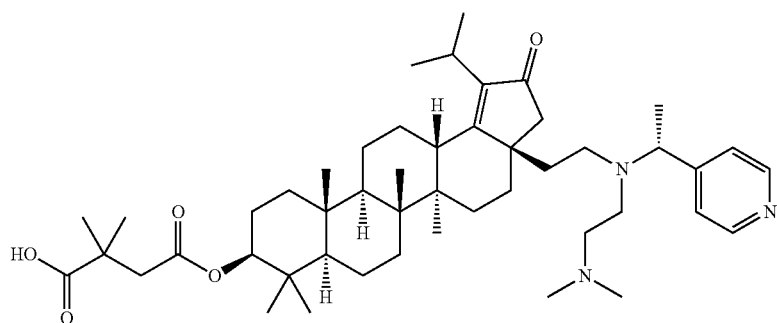
Example 462

550

Compound 531

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((2-(dimethylamino)ethyl)((R)-1-(pyridin-4-yl)ethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



531

LC/MS: m/z calculated 773.6. found 774.7 (M+1)⁺

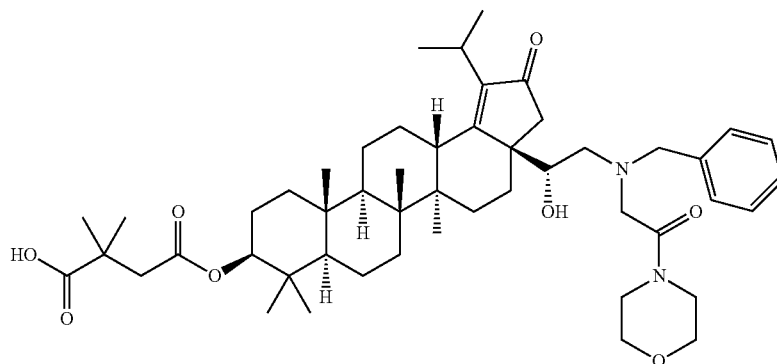
Example 463

35

Compound 532

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(benzyl(2-morpholino-2-oxoethyl)amino)-1-
hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40



532

LC/MS: m/z calculated 830.5. found 831.5 (M+1)⁺

551

Example 464

552

Compound 533

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((cyclopentylmethyl)amino)ethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

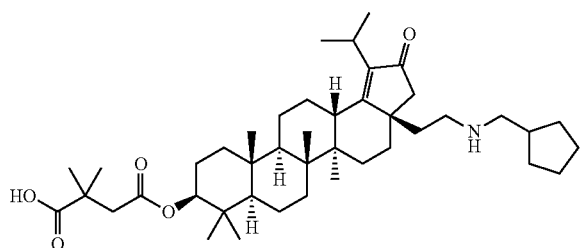
10

15

533

20

25



LC/MS: m/z calculated 679.5. found 680.7 (M+1)⁺

30

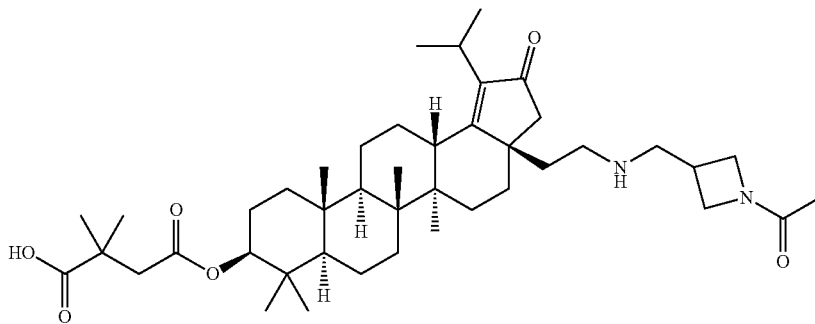
Example 465

Compound 534

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(((1-acetylazetidin-3-yl)methyl)amino)ethyl)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

35

534



LC/MS: m/z calculated 708.5. found 709.7 (M+1)⁺

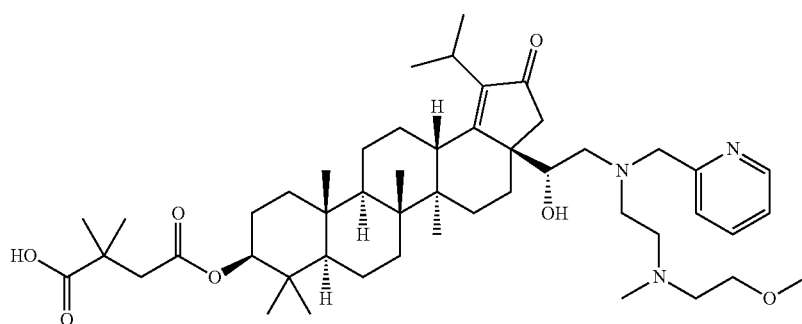
Example 466

Compound 535

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-1-hydroxy-2-((2-((2-methoxyethyl)(methyl)
 amino)ethyl)(pyridin-2-ylmethyl)amino)ethyl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

5

10



535

LC/MS: m/z calculated 819.6. found 820.5 (M+1)⁺

35

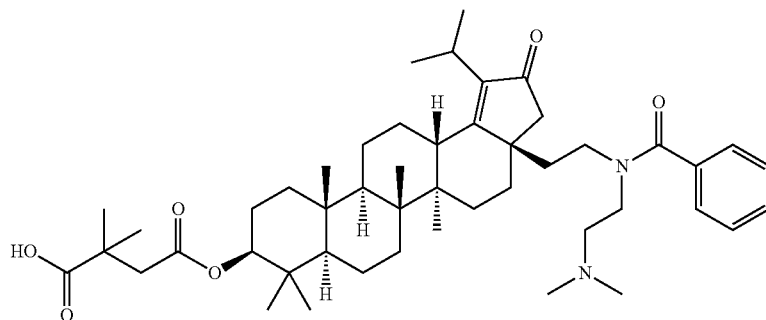
Example 467

Compound 536

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 (N-(2-(dimethylamino)ethyl)benzamido)ethyl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

40

45



536

LC/MS: m/z calculated 772.5. found 773.5 (M+1)⁺

555

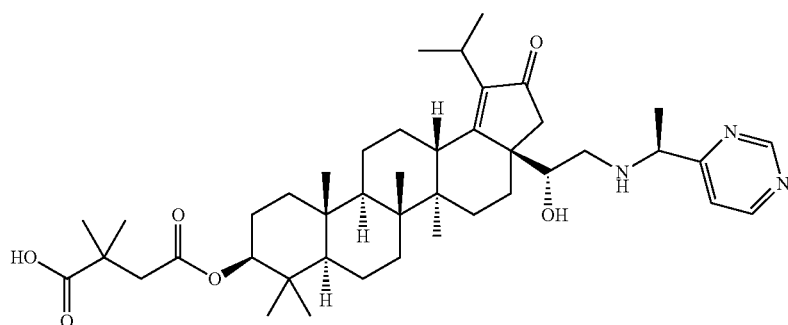
Example 468

556

Compound 537

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(((S)-1-(pyrimidin-4-yl)ethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



537

LC/MS: m/z calculated 719.5. found 720.5 (M+1)⁺

35

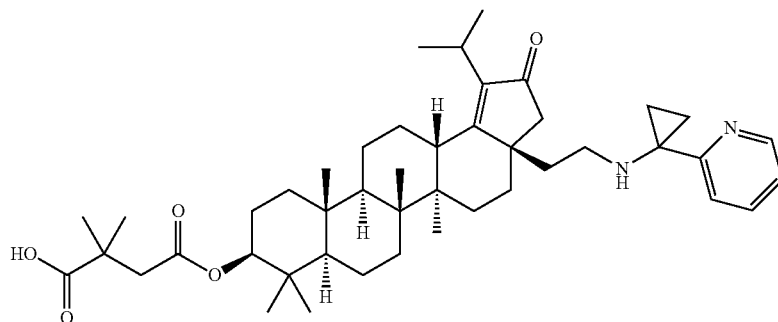
Example 469

Compound 538

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((1-
(pyridin-2-yl)cyclopropyl)amino)ethyl)-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



538

LC/MS: m/z calculated 714.5. found 715.5 (M+1)⁺

557

558

Example 471

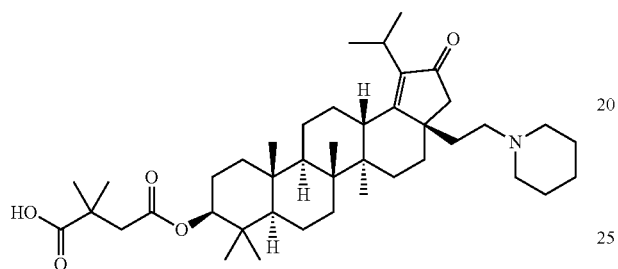
Compound 540

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-(pip-
eridin-1-yl)ethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5

10

540 15



25

30

LC/MS: m/z calculated 665.5. found 666.5 (M+1)⁺

Example 472

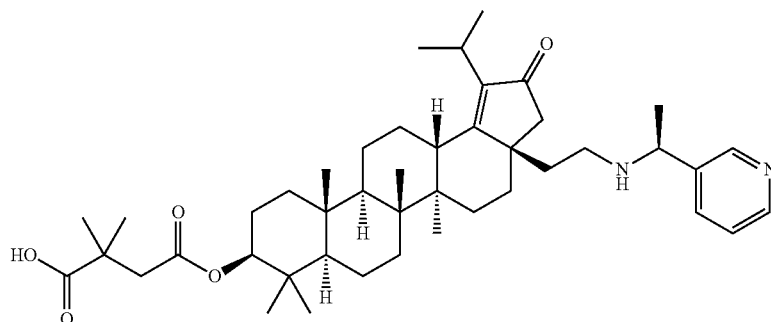
35

Compound 541

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-(((S)-
1-(pyridin-3-yl)ethyl)amino)ethyl)-3,3a,4,5,5a,5b,6,
7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

541



LC/MS: m/z calculated 702.5. found 703.4 (M+1)⁺

559

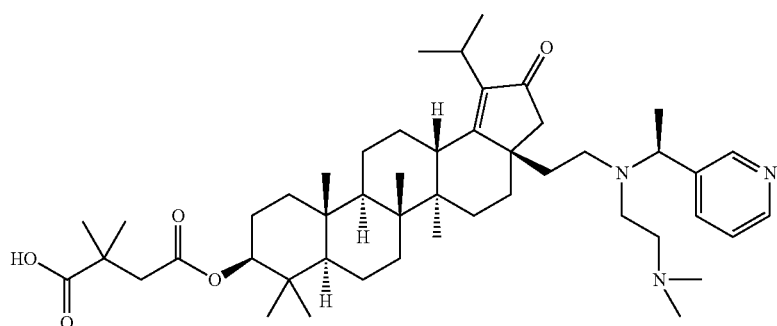
Example 473

560

Compound 542

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((2-(dimethylamino)ethyl)((S)-1-(pyridin-3-yl)ethyl)
 amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



542

LC/MS: m/z calculated 773.6. found 774.7 (M+1)⁺

35

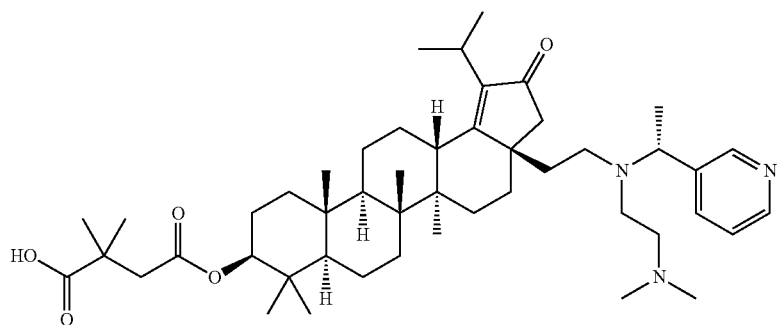
Example 474

Compound 543

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
 ((2-(dimethylamino)ethyl)((R)-1-(pyridin-3-yl)ethyl)
 amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
 ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
 12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
 9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



543

LC/MS: m/z calculated 773.6. found 774.7 (M+1)⁺

561

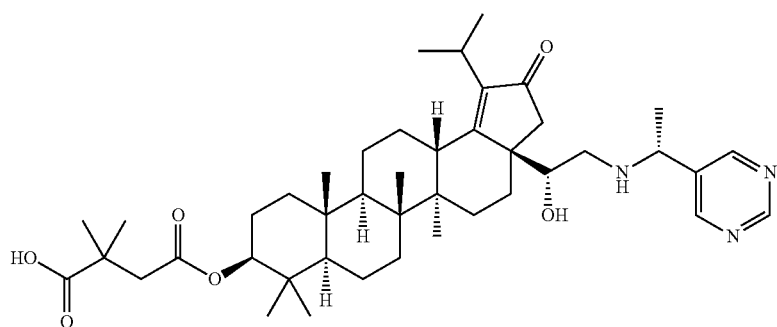
Example 475

562

Compound 544

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-1-hydroxy-2-(((R)-1-(pyrimidin-5-yl)ethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



544

LC/MS: m/z calculated 719.5. found 719.8 (M+1)⁺

35

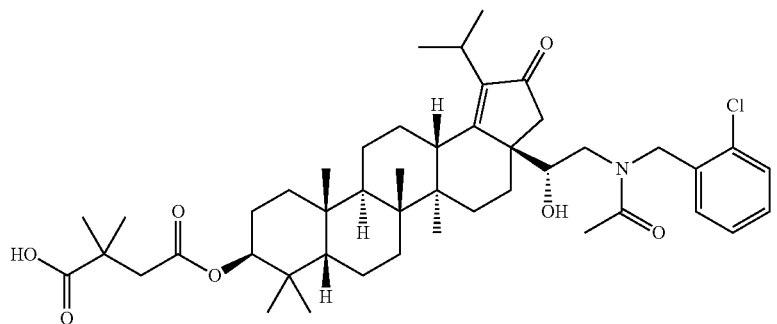
Example 476

Compound 545

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-(N-(2-chlorobenzyl)acetamido)-1-hydroxy-
ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-
3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



545

LC/MS: m/z calculated 779.4. found 780.3 (M+1)⁺

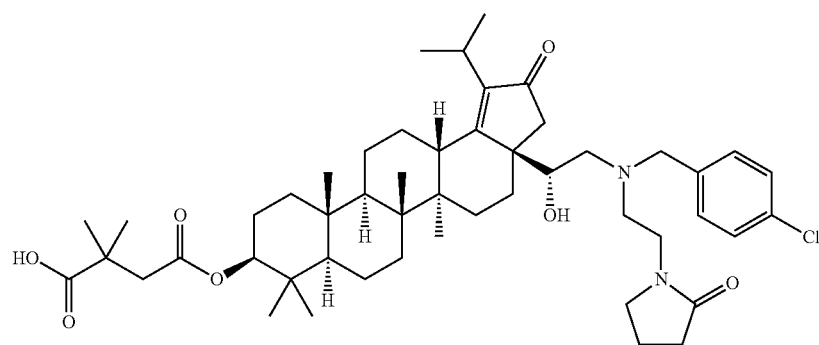
563

564

Example 477

Compound 546

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((4-chlorobenzyl)(2-(2-oxopyrrolidin-1-yl)
 ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
 acid 5 10



546

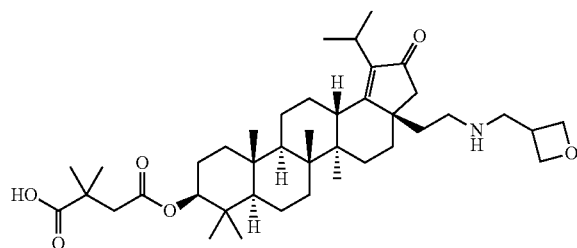
LC/MS: m/z calculated 848.5. found 849.5 (M+1)⁺

Example 478

35

Compound 547

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
 propyl-5a,5b,8,8,11a-pentamethyl-3a-(2-((oxetan-3-
 ylmethyl)amino)ethyl)-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
 8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
 cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
 oxobutanoic acid 40 45



547

50

55

60

65

LC/MS: m/z calculated 667.5. found 668.4 (M+1)⁺

565

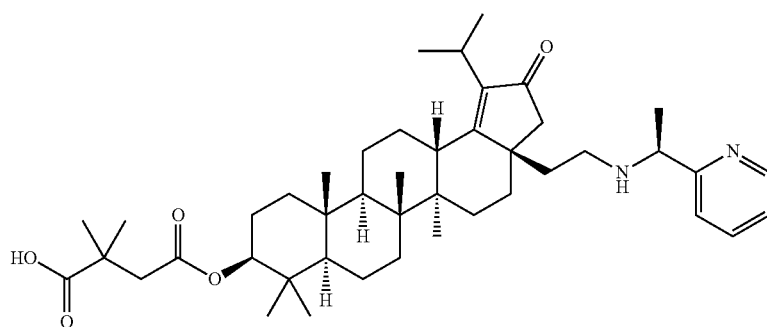
Example 479

566

Compound 548

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-(((S)-
1-(pyridin-2-yl)ethyl)amino)ethyl)-3,3a,4,5,5a,5b,6,
7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5



548

LC/MS: m/z calculated 702.5. found 703.5 (M+1)⁺

35

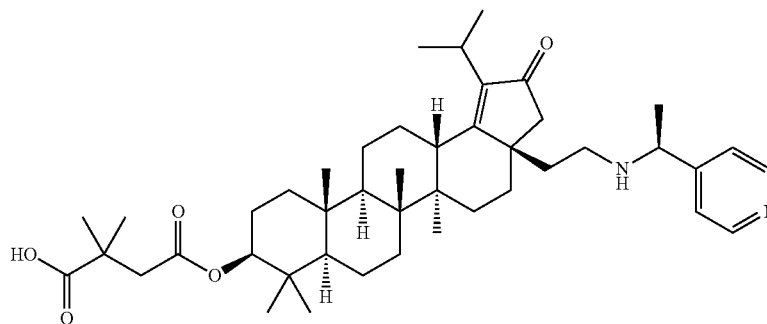
Example 480

Compound 549

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-(((S)-
1-(pyridin-4-yl)ethyl)amino)ethyl)-3,3a,4,5,5a,5b,6,
7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-
2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

40

45



549

LC/MS: m/z calculated 702.5. found 703.4 (M+1)⁺

567

Example 481

568

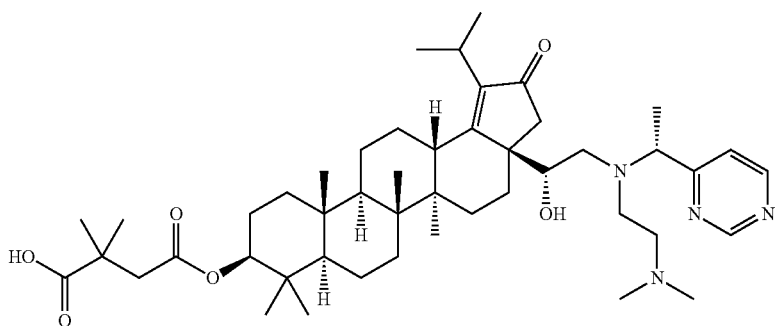
Compound 550

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)((R)-1-(pyrimidin-
4-yl)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,
5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

5

10

550



LC/MS: m/z calculated 790.6. found 791.5 (M+1)⁺

35

Example 482

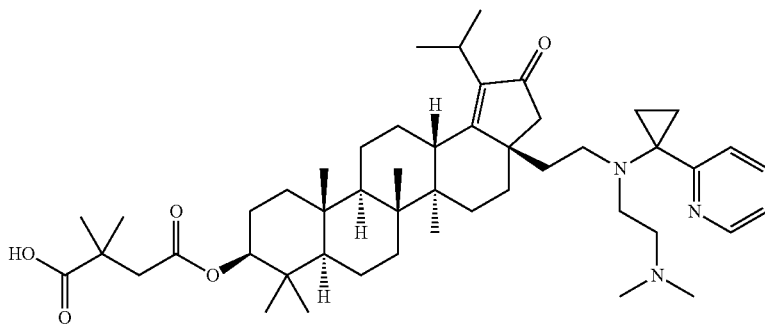
Compound 551

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((2-(dimethylamino)ethyl)(1-(pyridin-2-yl)cyclopro-
pyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45

551



LC/MS: m/z calculated 785.6. found 786.5 (M+1)⁺

569

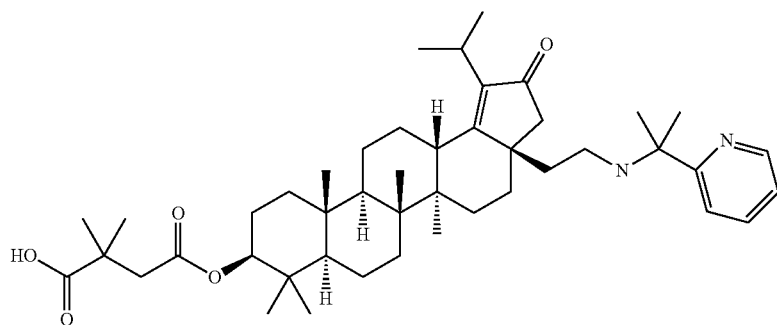
570

Example 483

Compound 552

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((2-
(pyridin-2-yl)propan-2-yl)amino)ethyl)-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



552

LC/MS: m/z calculated 716.5. found 717.5 (M+1)⁺

35

Example 484

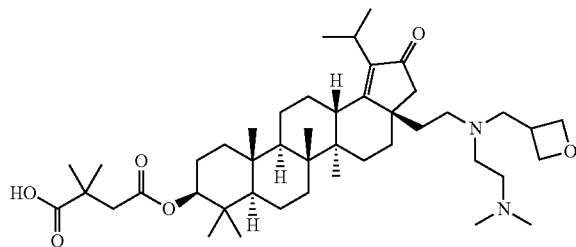
Compound 553

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((2-(dimethylamino)ethyl)(oxetan-3-ylmethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

45

50

553



55

60

65

LC/MS: m/z calculated 738.5. found 739.5 (M+1)⁺

571

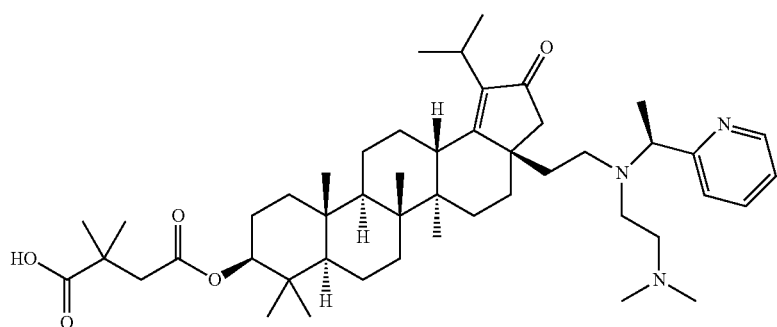
Example 485

572

Compound 554

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((2-(dimethylamino)ethyl)((S)-1-(pyridin-2-yl)ethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



554

LC/MS: m/z calculated 773.6. found 774.5 (M+1)⁺

35

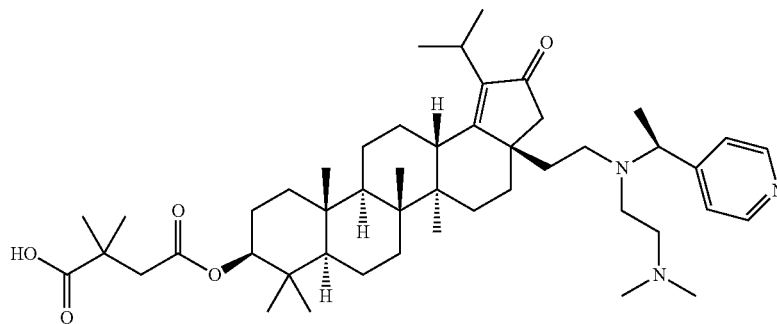
Example 486

Compound 555

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((2-(dimethylamino)ethyl)((S)-1-(pyridin-4-yl)ethyl)
amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



555

LC/MS: m/z calculated 773.6. found 774.5 (M+1)⁺

573

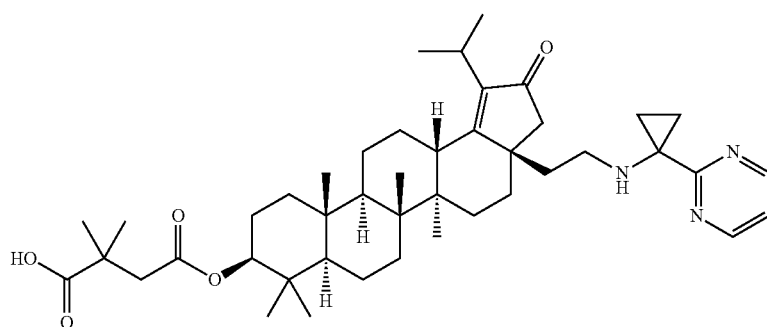
Example 487

574

Compound 556

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((1-(pyrimidin-2-yl)cyclopropyl)amino)ethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



556

LC/MS: m/z calculated 715.5. found 716.5 (M+1)⁺

35

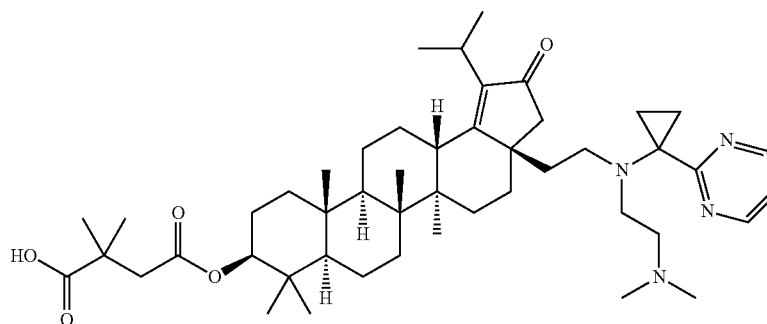
Example 488

Compound 557

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-((2-(dimethylamino)ethyl)(1-(pyrimidin-2-yl)cyclopropyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



557

LC/MS: m/z calculated 786.6. found 787.5 (M+1)⁺

575

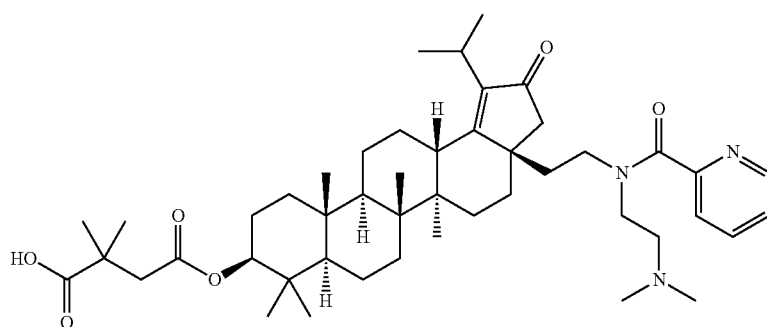
Example 489

576

Compound 558

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
(N-(2-(dimethylamino)ethyl)picolinamido)ethyl)-1-
isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

5



558

LC/MS: m/z calculated 773.5. found 774.5 (M+1)⁺

35

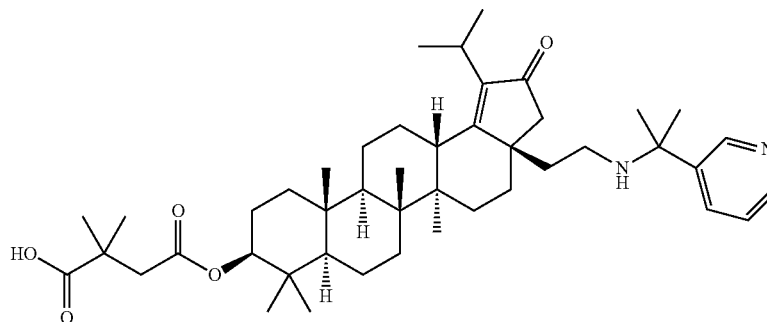
Example 490

Compound 559

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-iso-
propyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((2-
(pyridin-3-yl)propan-2-yl)amino)ethyl)-3,3a,4,5,5a,
5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
2,2-dimethyl-4-oxobutanoic acid

40

45



559

LC/MS: m/z calculated 716.5. found 717.5 (M+1)⁺

577

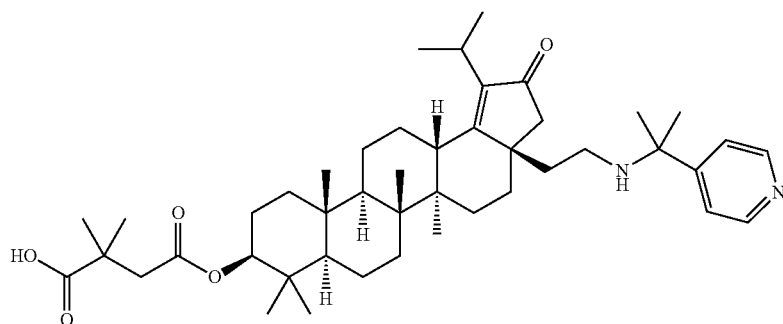
Example 491

578

Compound 560

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3a-(2-((2-(pyridin-4-yl)propan-2-yl)amino)ethyl)-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



560

LC/MS: m/z calculated 716.5. found 717.5 (M+1)⁺

Example 492

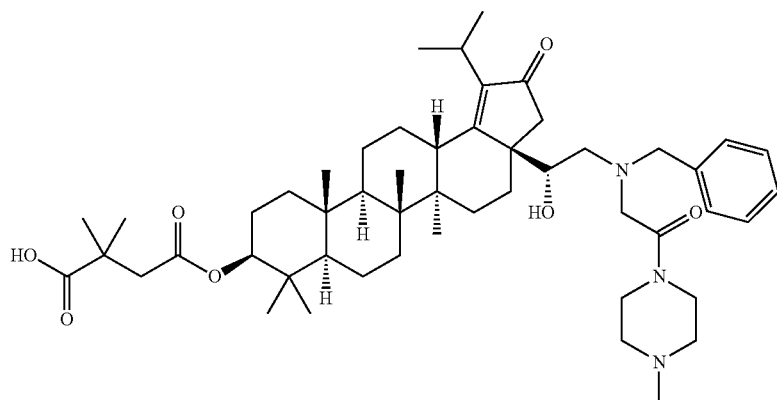
35

Compound 561

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(benzyl(2-(4-methylpiperazin-1-yl)-2-oxoethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

40

45



561

LC/MS: m/z calculated 843.6. found 844.5 (M+1)⁺

579

580

Example 493

Compound 562

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(oxazol-4-ylm-
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

5

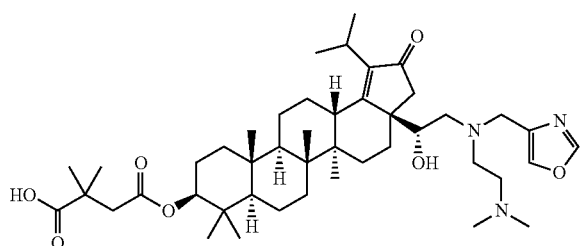
10

15

562

20

25



LC/MS: m/z calculated 765.5. found 766.5 (M+1)⁺

30

Example 494

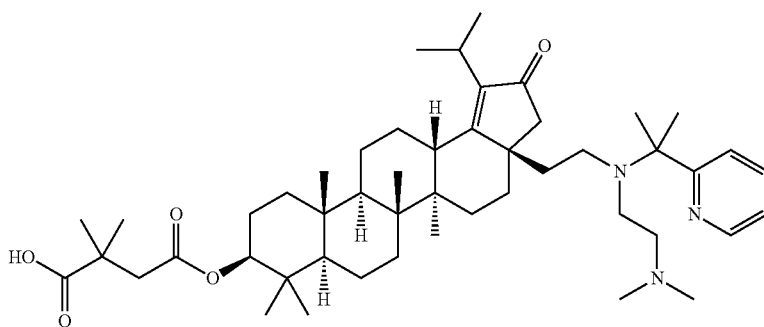
Compound 563

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((2-(dimethylamino)ethyl)(2-(pyridin-2-yl)propan-2-
yl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pentam-
ethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

35

40

563



LC/MS: m/z calculated 787.6. found 788.5 (M+1)⁺

581

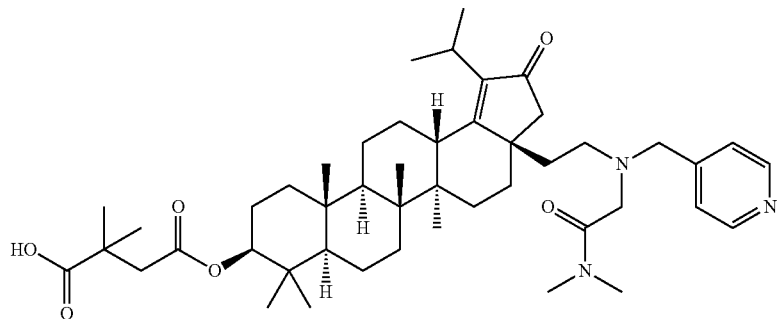
Example 495

582

Compound 564

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-(2-
((2-(dimethylamino)-2-oxoethyl)(pyridin-4-ylm-
ethyl)amino)ethyl)-1-isopropyl-5a,5b,8,8,11a-pen-
tamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,
11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

5



564

30

LC/MS: m/z calculated 773.6. found 774.5 (M+1)⁺

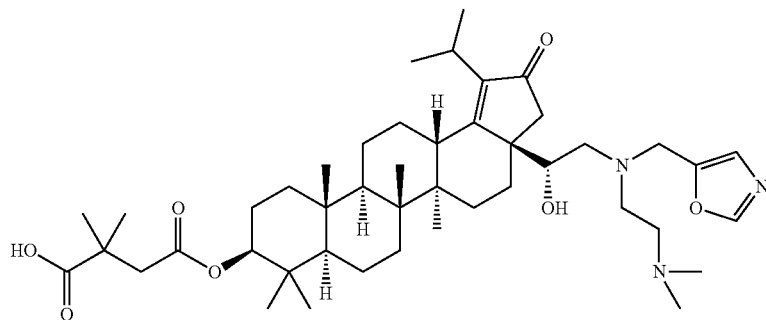
Example 496

Compound 565

35

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(oxazol-5-ylm-
ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic
acid

40



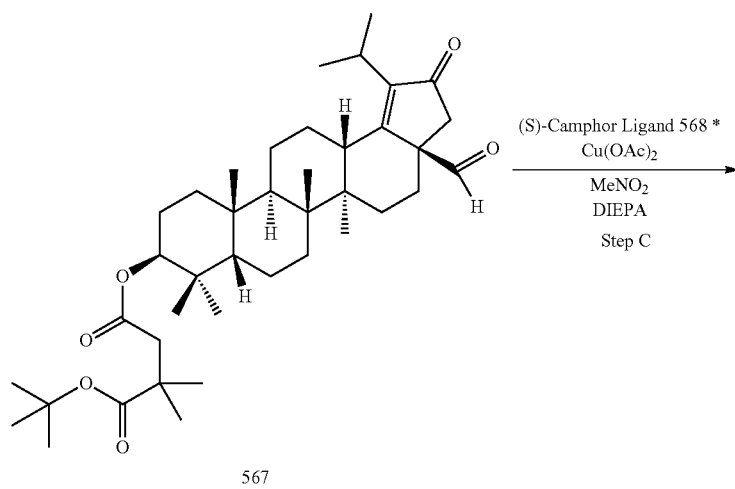
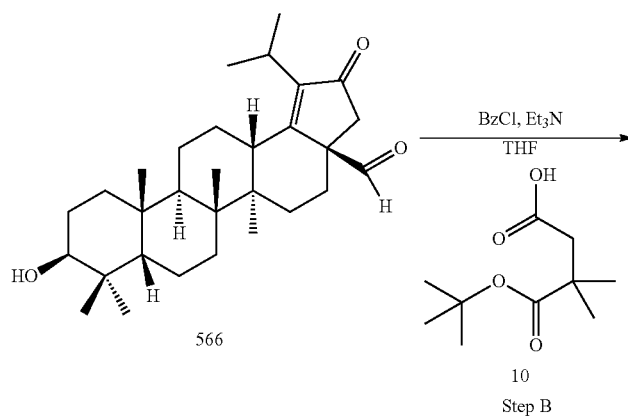
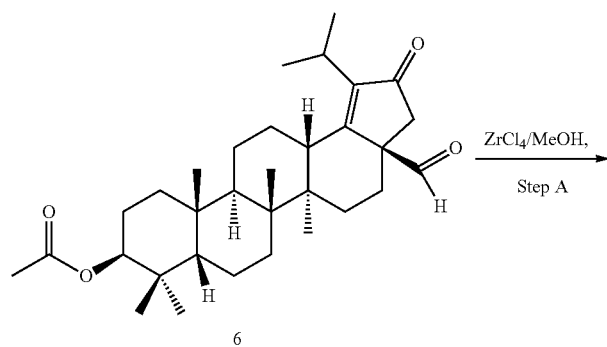
565

LC/MS: m/z calculated 765.5. found 766.5 (M+1)⁺

583

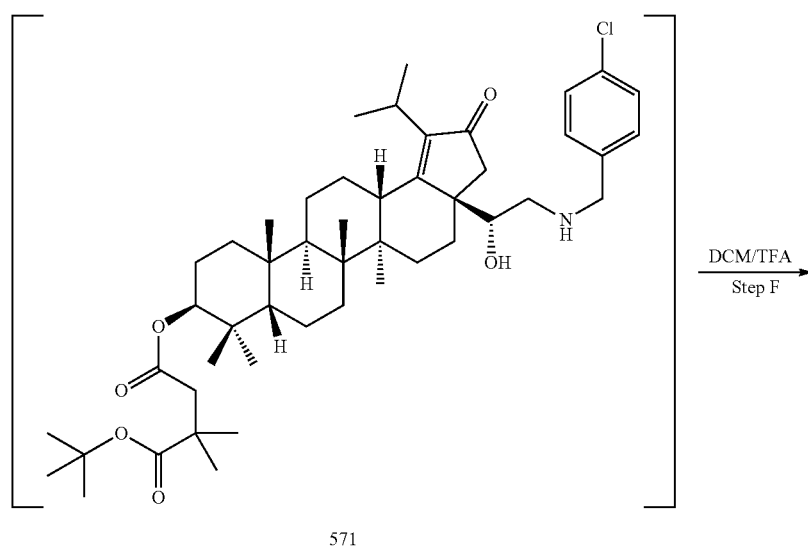
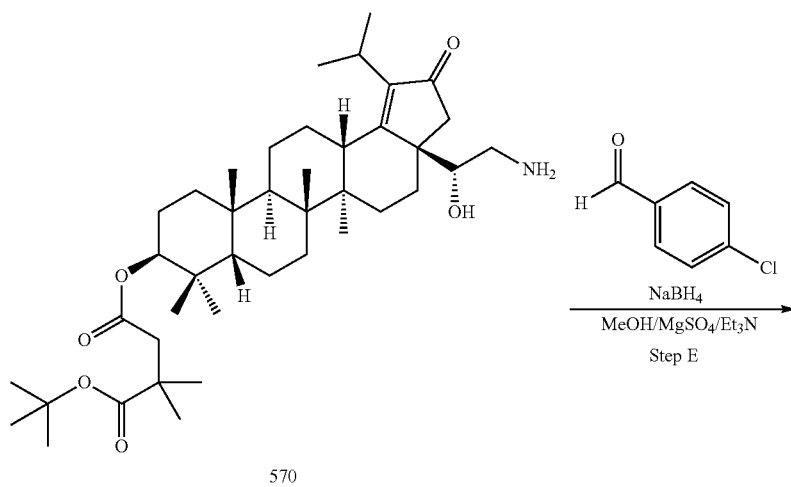
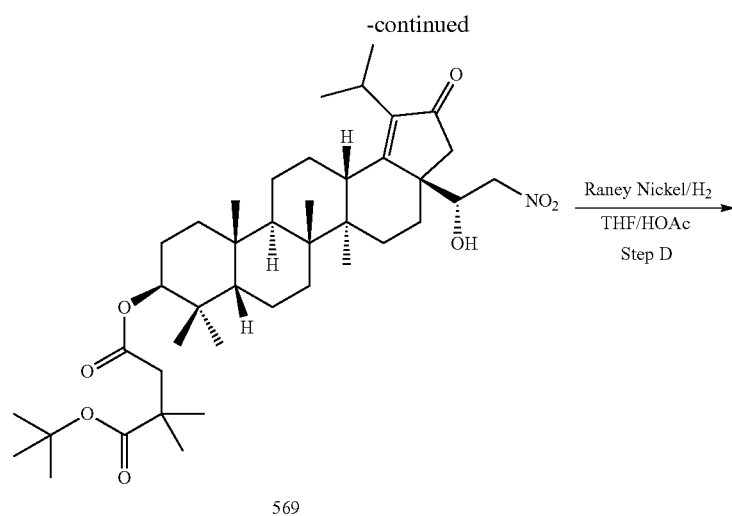
Example 497

Compound 46

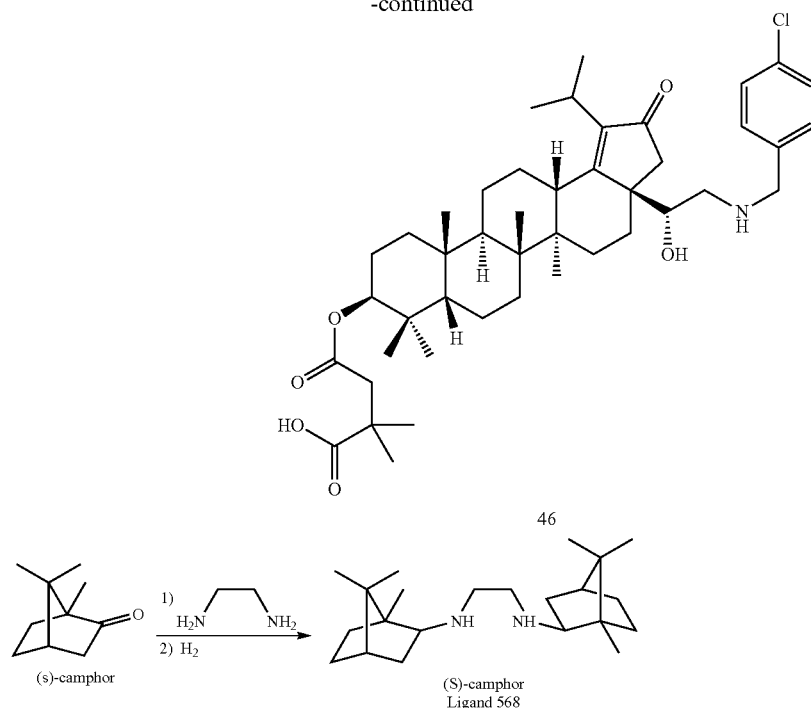


585

586



-continued



Step A: Intermediate 566

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysene-3a-carbaldehyde

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-Formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (50 g) placed in a round bottomed flask with methanol (500 ml, 10 vol) and DCM ("dichloromethane"-200 ml, 4 vol) and stirred at ambient temp while adding solid $ZrCl_4$ (23.4 g, 1 equiv.) in portions.

The reaction was warmed to approximately 60° C. and maintained for a total of 16 hours. The reaction was monitored for completion on HPLC (starting material and product formed an acetal derivative during the reaction). Once complete, the reaction was treated with water (5 equiv.) and maintained at 60 degrees for approximately 30 minutes.

Next, the reaction was cooled and evaporated under vacuum at a bath temp of approximately 40° C. to 200 ml (4 volumes). Ethyl acetate (500 ml, 10 vol) was added and reaction was then treated with 1N HCl (250 ml, 5 vol). The reaction was then mixed thoroughly and the layers were allowed to separate. The lower aqueous layer was drained off and back-washed with fresh ethyl acetate (100 ml, 2 vol).

The combined organic layer was washed with 1N HCl (250 ml, 5 vol) and evaporated under vacuum at a bath temp of 40° C. to 200 ml (4 vol) and then treated with acetonitrile (500 ml, 10 vol). The reaction was then evaporated to a final volume of approximately 150 ml (3 vol). Acetonitrile (500 ml, 10 vol) was then added and the reaction was warmed to a 60° C. forming solution. Next, was slowly added 3N HCl (100 ml, 2 vol), which resulted in precipitate formation. (see note 2). The reaction was then allowed to cool to ambient temperature and then it was filtered. The filtrated solid was next rinsed with acetonitrile (2 vol) and dried in vacuo to give a weight of 33.0

g, 72% yield of (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysene-3a-carbaldehyde.

Note 1: The isolated solids were contaminated with a small amount of dimethyl acetal of product, which required reslurry in hot acetonitrile/3N HCl to complete the hydrolysis and resulted in loss of product (27 g recovered on re-treatment). It was determined that in process monitoring of reaction slurries during final hydrolysis require filtration of reaction aliquot in order to observe remaining dimethyl acetal. Dissolution of crude acetonitrile/aqueous HCl reaction solution for HPLC monitoring results in artificially low observed levels of dimethyl acetal due to hydrolysis in sample prep.

Note 2: Preferred procedure would be to add a portion of the 3N HCl (0.5 vol) and maintain reaction in solution at approximately 60° C. until dimethyl acetal hydrolysis is complete followed by addition of remainder (1.5 vol) of the 3N HCl and cooling to ambient temperature for filtration. Expected yield is 72%.

Step B: Intermediate 567

1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-Hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysene-3a-carbaldehyde (26.9 g, 1 equiv), 4-(tert-butoxy)-3,3-dimethyl-4-oxobutanoic acid (14.96 g, 1.25 equiv) and THF (538 ml, 20 vol) were charged to a flask. Benzoyl chloride (10.4 g, 1.25 equiv) was added followed by slow addition of triethylamine (14.97 g, 2.5 equiv) forming a thick slurry. DMAP (0.181 g, 0.25 equiv) was added and the reaction was allowed to stir at ambient temperature for

589

approximately 18 hours until complete by HPLC. Reaction was then charged with ethyl acetate (538 mL, 20 vol) and water (269 mL, 10 vol), stirred well and allowed to settle. Aqueous phase was removed and the organic phase washed with saturated sodium bicarbonate solution (2×10 vol) followed by water (269 mL, 10 vol). The reaction solution evaporated under vacuum to approximately 4 volumes to produce solids. Additional hexanes (269 mL, 10 vol) was added and reaction heated back to reflux to nearly form solution and slowly cooled to ambient temperature (seeding with desired product) and let stir for 15 minutes then cooled to 0° C. for approximately two hours and filtered solid. Washed solid with hexanes (2×10 vol) and dried at 50° C. under vacuum to a weight of 32.15 g, 85% yield of 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate.

Step C: Intermediate 569

1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

The reaction was charged with 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (15.75 g, 1 equiv), tert-butanol (157 mL, 10 vol) and toluene (47 mL, 3 vol) and stirred at ambient temperature. The ligand (N1,N2-bis(1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)ethane-1,2-diamine, derived from (S)-camphor, 0.492 g, 0.06 equiv) and copper (II) acetate mono hydrate (0.246 g, 0.05 equiv) were added in a single portion and reaction allowed to stir at ambient temperature for at least 2.5 hours (see note 1). The reaction is charged with nitromethane (7.52 g, 5 equiv) and Hunig's base ("N,N-diisopropylethylamine"-3.82 g, 1.2 equiv) and allowed to stir at ambient temperature for approximately 5 days. (See note 2). Reaction concentrated under vacuum at bath temp of no more than 35° C. to approximately 2 vols. (See note 3). Reaction charged with toluene (236 mL, 15 vols) and concentrated under vacuum again to approx 3 vols. Additional toluene (95 mL, 3 vol) was added to achieve a final reaction volume of approx 6 vols. Heptane (158 mL, 10 vols) was added slowly of to solution. Product began to crystallize out of solution upon seeding. Reaction was allowed to stir at ambient temperature for one to two hours and solids collected by filtration and washed with 10 vols of heptane. Solids were dried to a weight of 14.3 g (83% yield). Purity of isolated solid is typically ~90-95% with a 98/2 diastereomeric ratio favoring 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate as the major diastereomer.

Step D: Intermediate 570

4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-amino-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate

1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a,5b,8,8,11a-

590

pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (12.9 g, 18.4 mmol) was placed in 1-L retreat curve impeller reactor and then added 22 vol of 90% THF-HOAc and stirred to dissolve at ambient temp. The reactor was purged 3× with nitrogen and then a slurry of water was added and then washed (pH ~8-9) RaNi catalyst (50% water, added 2.6 mL catalyst slurry, 1.3 g RaNi calculated) and then placed under hydrogen at 0.3 bar pressure for 3 hours and then raised the pressure to 2 bar and allowed to stir for 18 hours. Reaction was approximately 20% complete at this time. The temperature was raised to 35 deg C. and then the reaction was stirred for another 7 hours and sampled. The reaction was approximately 31% complete at this time. Reaction pressure was increased to 4 bar hydrogen and was allow to continue stirring at 35 deg for 20 hours. Reaction is 75% complete at this time and no change in impurity profile. Added another 0.15 wt of RaNi (3.0 mL of 50% slurry) to bring total RaNi loading up to 25 wt % and the reaction was allowed to stir at 35 deg under 4 bar Hydrogen for another 24 hours. The reaction was then determined to be complete by HPLC.

The reaction was then filtered through a 4 micron in-line filter, rinsing with THF (50 mL). Evaporated to approximately 3 vol and added ethyl acetate (195 mL, vol) and washed with 1N NaOH solution (3×10 vol) and verified final wash to be basic pH. (Note: addition of 0.5 vol saturated NaCl solution was required on second and third washes to obtain efficient separation). Washed with saturated sodium chloride solution (5 vol) and evaporated to a solid foam that was azeotroped with 2×5 vol dichloromethane in order to obtain a solid foam. Dried on high vacuum pump to weight of 11.1 g (90% yield).

Recrystallized above sample (10.5 g) by dissolving in methanol (147 mL, 14 volumes) at reflux and then cooling with seeding to ambient temperature and allowed to stir 30 minutes). Mixture was further cooled to 15 degrees and filtered. Solids collected by filtration and washed with methanol (1 volume) and dried at 50 degrees in vacuo to a weight of 7.5 g (71% yield on recrystallization) of 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-amino-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate.

Step E and F: Compound 46

1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-Amino-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate and p-Cl-benzaldehyde (1.1 equiv) were placed in a round bottomed flask with EtOH (10 vol) and added Na₂CO₃ powder (2.5 equiv) and allowed to stir overnight (16 hrs). The next day, the reaction slurry was cooled to approximately 10 degrees and added NaBH₄ to the reaction in a single portion and allowed reaction to stir while slowly warming to ambient temperature. Obtained HPLC after 45 minutes showing essentially complete conversion to desired product. p-Cl-benzyl alcohol present as well (using 220 nm wavelength). The reaction was then diluted with methylene chloride (30 mL, 10 vol) and water (30 mL, 10 vol) and the layers were allowed to separate. The DCM layer was then washed with additional water (10 vol) and evaporated to

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minimum volume on rotovap and added back DCM (10 vol) and treated with trifluoroacetic acid (6 ml, 2 vol) and the reaction was allowed to stir at ambient temperature. The reaction was almost complete after one hour, but it was left to stir overnight. After 18 hours reaction complete by HPLC and was evaporated to an oil.

Dissolved with warming to approximately 45 degrees in ethyl acetate (60 ml, 20 vol) and washed with NaHCO_3 solution (2x10 vol) to remove residual TFA. Then, washed with ethyl acetate and with half-saturated NaCl solution and evaporated to dryness and azeotroped dry with isopropanol (2x5 vol). Dissolved in isopropanol (5 vol) and diluted with acetonitrile to cloud point (10 vol) and then allowed to crystallize overnight. Cloudy mixture, but no filterable solids present. Meanwhile the test crystallization from ethyl acetate-heptane of the original isolated TFA salt solution had produced nice solids.

The entire reaction was then evaporated to dryness and azeotroped several portions of ethyl acetate on rotovap (3x10 vol) to remove all isopropanol and acetonitrile. Reaction dissolved with warming to reflux in ethyl acetate (30 ml, 10 vol). Added one equivalent trifluoroacetic acid (0.51 g) and slowly diluted with heptane to cloud point (15 ml, 3 volumes). Seeded with test crystallization seeds from above. Nice solids resulted almost immediately. Stirred with cooling to ambient temperature. Filtered solids and washed with heptane (15 ml, 3 vol). Dried on funnel to weight of 2.55 g, 67% yield of 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid.

Alternative Procedure

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-Amino-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)1-tert-butyl 2,2-dimethylsuccinate (7 g, 1 equiv.) was placed in a round bottom flask and added MgSO_4 powder (2.5 equiv) and Et_3N (0.8 equiv) and p-Chlorobenzaldehyde and added

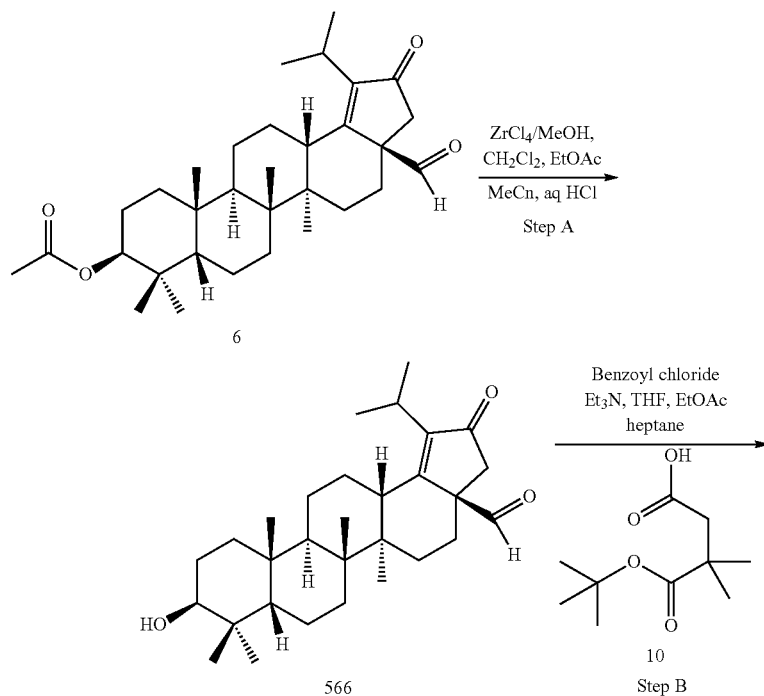
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MeOH (10 vol) and allowed to stir overnight (16 hrs). After this time an aliquot (0.5 ml) of the white slurry was removed and treated with approximately 25 mg NaBH_4 and allowed to stir for 5 minutes. Obtained HPLC of this aliquot indicating complete consumption of the amine starting material. The reaction mixture was cooled to 0 degrees on ice-brine bath and treated with solid NaBH_4 in a single portion (475 mg, 1.2 equiv) and allowed to stir at 0 degrees for approximately 45 minutes. HPLC after this time shows reaction is complete. The reaction was warmed to ambient temperature briefly and filtered through a CELITE® bed. The solid was rinsed with additional methanol (35 ml, 5 vol) and then dichloromethane (70 ml, 10 vol). The filtrate/rinse was then treated with water (70 ml, 10 vol) and shaken in separatory funnel. The upper aqueous was washed well with additional dichloromethane (3x5 vol) and then the combined organic layers were washed with brine (10 vol). The organic phase was evaporated to a solid foam and azeotroped with dichloromethane. Dissolved in dichloromethane (70 ml, 10 vol) and treated with trifluoroacetic acid (14 ml, 2 vol) and allowed to stir at ambient temperature. The reaction almost complete in approximately 2 hours.

The reaction was allowed to sit over a weekend at which point the reaction was complete. The reaction was allowed to evaporate to a minimum volume and then ethyl acetate (10 vol) was added and evaporated to a minimum volume again. Repeated this evaporating to minimum volume and then dissolved in total of volume ethyl acetate. Heated to near reflux and diluted with heptane (5 vol) and stirred while cooling to ambient temperature while solids were formed. Stirred for 30 minutes and filtered. Rinsed with heptane (3 vol) and dried to a weight of 4.85 g, 63% yield of 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid over two steps.

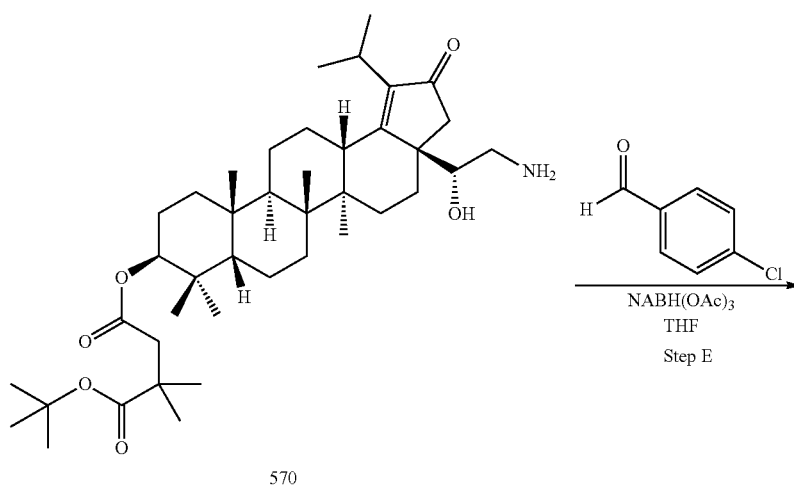
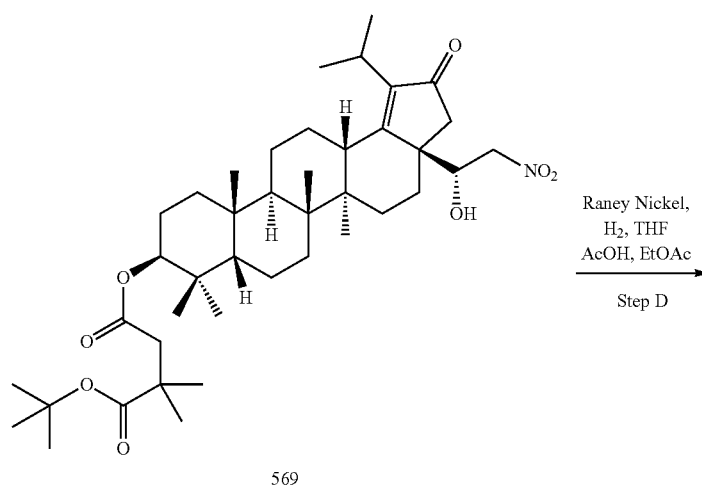
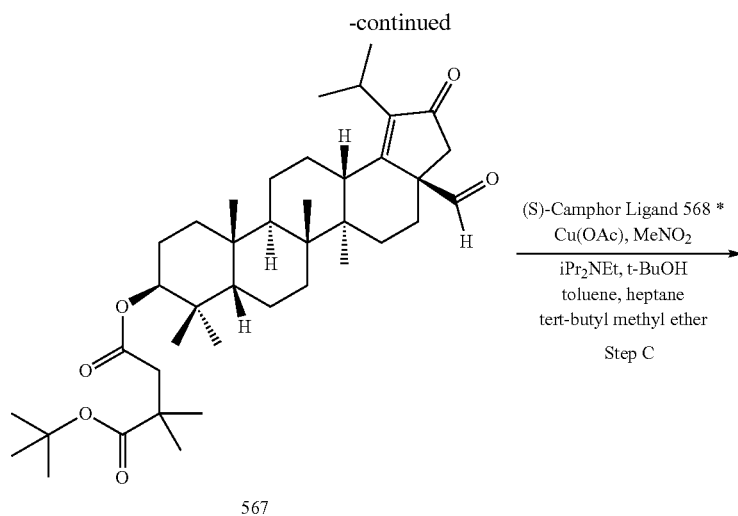
Example 498

Compound 51



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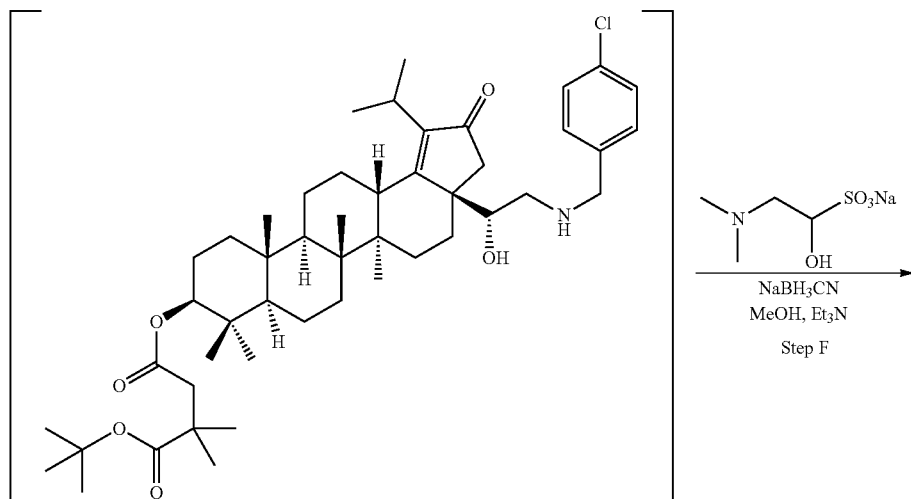
594



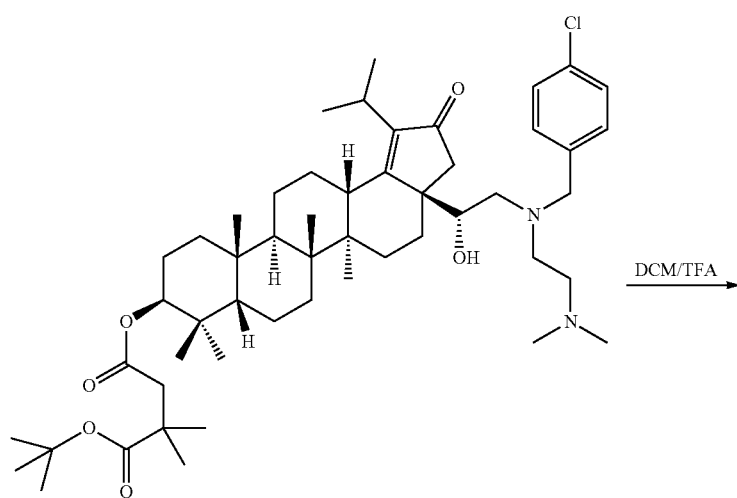
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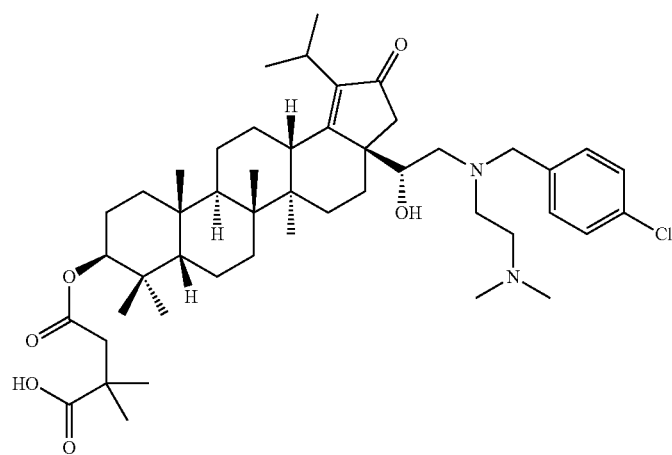
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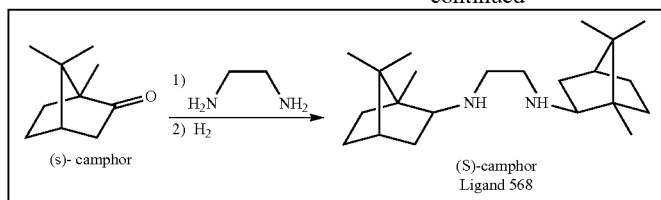


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Step A: Intermediate 566

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysene-3a-carbaldehyde

The compound (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (400 g, 0.81 mol) was placed in a flask with methanol (4 L) and DCM (1.6 L) and stirred at ambient temp while adding solid ZrCl_4 (225.2 g, 0.97 mol) in portions. The reaction was warmed to approximately 45–55° C. and maintained for a total of 30–36 hours. The reaction was monitored for completion by HPLC.

Once complete, the reaction was then treated with water (120 mL) and maintained at 45–55° C. for approximately 30–60 minutes. The reaction was then cooled and evaporated under vacuum (at bath temp approximately 40° C.) to 1200 mL. Dichloromethane (4 L) was added and reaction was treated with 1N HCl (2 L), mixed thoroughly and the layers were allowed to separate. Afterwards, the upper aqueous layer was washed with fresh dichloromethane (800 mL). Next, the combined organic layer was washed with 1N HCl (2 L) and evaporated under vacuum (at bath temp of 40° C.) to 800 mL and treated with acetonitrile (4 L).

The reaction was then evaporated (at bath temp of 40° C.) to a final volume of approximately 800 mL. Acetonitrile (3.2 L) was added and the reaction was warmed to 50–60° C., thus forming a solution. Next was slowly added, 3N HCl (100 mL), which resulted in precipitate formation and which was maintained as a reaction in solution at approximately 50–60° C. until dimethyl acetal hydrolysis was complete followed by addition of water (4.8 L).

The reaction was allowed to cool to 0–100° C. and then the mixture was filtered and the resultant solid was rinsed with acetonitrile/water (1/1,800 mL). The solid was then slurried in 10 volumes of heptane at 85–100° C. for 1–3 hours. The slurry was then cooled to ambient temperature and filtered. Washed the cake with 800 mL heptane then dried in vacuo at 40–50° C. to the 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate 286 g. Yield is 72.6% corrected by assay.

^1H NMR (400 MHz, CDCl_3) δ =9.33 (s, 1H), 3.20–3.28 (m, 2H), 2.57 (d, J=1H), 2.36–2.42 (m, 2H), 2.04–2.08 (m, 2H), 1.86–1.90 (m, 2H), 1.75–1.78 (m, 1H), 1.23–1.66 (m, 35H); LC/MS: m/z calculated 454.3. found 455.4 (M+1)⁺

Step B: Intermediate 567

1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

The starting material (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-

oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysene-3a-carbaldehyde (32.4 g, 71 mmol), 4-(tert-butoxy)-3,3-dimethyl-4-oxobutanoic acid (18 g, 89 mmol) and THF (648 mL) were charged to a flask. Benzoyl chloride (12.5 g, 89 mmol) was added followed by slow addition of triethyl amine (18 g, 178 mmol) forming a thick slurry. DMAP (2.17 g, 18 mmol) was added and the reaction was allowed to stir at ambient temperature for approximately 24–30 hours until complete by HPLC. The reaction was then charged with ethyl acetate (648 mL) and water (324 mL), stirred well and allowed to settle. The aqueous phase was removed and the organic phase washed with saturated sodium bicarbonate solution (2×324 mL) followed by water (324 mL).

The reaction solution was then evaporated under vacuum to approximately 129 mL in order to produce solids. Additional heptane (324 mL) was added and the reaction heated back to reflux to a nearly formed solution and slowly cooled to ambient temperature and was stirred for 15 minutes then cooled to 0° C. for approximately two hours and the solids were filtered. The solids were then washed with heptane (2×324 mL) and dried at 50° C. under vacuum to give the desired compound as an off-white solid 1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate 36.8 g. yield is 80%. ^1H NMR (400 MHz, CDCl_3) δ =9.24 (s, 1H), 4.41–4.45 (m, 1H), 3.19–3.20 (m, 1H), 2.33–2.48 (m, 5H), 0.96–1.60 (m, 37H), 0.77–0.87 (m, 17H); LC/MS: m/z calculated 638.4. found 639.4 (M+1)⁺.

Step C: Intermediate 569

1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

The reaction was charged with of 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (50 g, 78 mmol), tert-butanol (500 mL) and toluene (150 mL) and the temperature was adjusted to 20–25° C. The ligand (N1,N2-bis(1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)ethane-1,2-diamine (1.56 g, 4.7 mmol) and Copper(I) acetate (0.48 g, 3.9 mmol) were added in a single portion and the reaction was then stirred at 20–25° C. for 3–5 hrs.

The reaction was next allowed to cool to 7–13° C. The reaction was then charged with nitromethane (33 g, 0.55 mmol) and N,N-diisopropyl ethylamine (12.1 g, 94 mmol) and allowed to stir at 7–13° C. for approximately 30 hrs. The reaction was again charged with nitromethane (17 g, 0.3 mmol) and allowed to stir at 7–13° C. for approximately hrs.

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The reaction was yet again charged with nitromethane (17 g, 0.3 mmol) and allowed to stir at 7-13° C. for approximately 20 hrs.

Next, the reaction was charged with MTBE (750 mL) and a 15% ammonium chloride solution (300 mL), allowed to stir for 30 min, and then separated into two phases. The organic phase was washed with water (250 mL) followed by brine (200 mL). The organic phase was then concentrated to 100 mL and MTBE (25 mL) was added. Next, n-heptane (500 mL) was slowly added and then stirred at 10-20° C. for 2 hrs. The reaction was then filtered and washed with n-heptane, and then dried under vacuum at 50-55° C. to give 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate as off-white solid 41.6 g. Yield is 75.9%, ¹H NMR (400 MHz, CDCl₃) δ=4.85 (bd, 1H), 4.51-4.55 (dd, 1H), 4.08-4.20 (m, 2H), 3.15-3.22 (m, 1H), 2.35-2.83 (m, 6H), 0.80-2.03 (m, 54H); LC/MS: m/z calculated 699.4, found 700.4 (M+1)⁺.

Step D: Intermediate 570

4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-amino-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 1-tert-butyl 2,2-dimethylsuccinate

To 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (30 g, 42.6 mmol) in THF (600 mL) and AcOH (30 mL) was added Raney Ni (30 g, 5%) under N₂ at room temperature. The reaction was stirred at 45-55° C. under hydrogen gas (0.30-0.40 MPa) for 10-12 hours. The reaction mixture was filtered through a filter aid, washing with THF [2×90 mL] and the filtrate was adjusted to a pH of 7-8 with 5% K₂CO₃ aqueous.

Next, ethyl acetate (450 mL) was added to the reaction mixture and the two phases were separated. The aqueous layer was extracted with ethyl acetate (150 mL). The combined organic phase was washed two times with 7.5% NaCl aqueous (300 mL) and then washed with 17% NaCl aqueous (300 mL). The organic phase was concentrated under vacuum to give 25.7 g of 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-amino-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 1-tert-butyl 2,2-dimethylsuccinate. Yield is 92%. ¹H NMR (400 MHz, DMSO-d₆) δ=4.40-4.44 (dd, 1H), 3.79-3.80 (bd, 1H), 3.59-3.62 (M, 2H), 3.12-3.17 (m, 2H), 2.60-2.75 (m, 1H), 2.22-2.34 (m, 2H), 2.19-2.22 (m, 2H), 1.37-1.84 (m, 25H), 1.08-1.11 (m, 17H), 0.81-0.91 (m, 13H); LC/MS: m/z calculated 669.5, found 670.4 (M+1)⁺.

Step E: Intermediate 571

1-tert-butyl 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

To a solution of 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-amino-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11,

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11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 1-tert-butyl 2,2-dimethylsuccinate in THF (5 g, 7.6 mmol in 100 mL THF) was added 4-chlorobenzaldehyde (0.96 g, 6.84 mmol) and then stirred at -2-2° C. for 0.5 hours. Next, NaHB(OAc)₃ (3.53 g, 16.7 mmol) was added to the reaction and stirred at -2-2° C. for 0.5 hours. The reaction was then warmed to 3-7° C. and again stirred at 3-7° C. for 10-15 hours and then stirred at 8-12° C. for 5-8 hours.

The reaction was quenched by saturated NH₄Cl (aqueous) (50 mL) and water (20 mL) and then stirred at 10-20° C. for 0.5 hours. The reaction was then extracted with MTBE (75 mL) and the aqueous layer was extracted with MTBE (25 mL). The combined organic phase was washed with water (25 mL) and the pH adjusted to 7-8 with 5% K₂CO₃ aqueous. The organic phase was separated and washed two times with 7.5% NaCl aqueous (50 mL) and then washed with 20% NaCl aqueous (50 mL). The organic phase was concentrated under vacuum again to approx 20 mL. Additional DCM (60 mL) was added and concentrated under vacuum to approx 20 mL. Additional DCM (60 mL) was again added and concentrated under vacuum to approx 20 mL. Additional DCM (60 mL) was again added and concentrated under vacuum to approx 20 mL. Then, 50 mL MeOH was charged and concentrated under vacuum again to approx 20 mL. An additional 50 mL MeOH was charged to give a solution of 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate in MeOH. This mixture was used in the next step directly. ¹H NMR (400 MHz, DMSO-d₆) δ=0.81-1.78 (m, 49H), 1.91 (s, 6H), 2.18-2.20 (m, 2H) 2.32-2.37 (m, 3H), 3.02-3.08 (M, 2H) 3.56-3.62 (m, 4H) 4.00-4.04 (d, 1H) 4.12-4.15 (d, 1H) 4.27-4.40 (m, 1H) 4.39-4.43 (m, 1H), 7.43-7.45 (d, 2H), 7.52-7.54 (d, 2H);

LC/MS: m/z calculated 793.5, found 794.4 (M+1)⁺.

Step F: Intermediate 54

1-tert-butyl 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

Added a solution of 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (55 g, 69.3 mmol) dissolved in methanol (825 mL), dimethyl amino acetaldehyde hydrogen sulfite sodium salt (66.8 g, 0.35 mol) and Et₃N (38.7 g, 0.38 mol) into a reactor. The reaction was stirred for 2-3 hrs at 30-40° C. under nitrogen protection. NaBH₃CN (8.8 g, 0.14 mol) was added and stirred at 30-40° C. under nitrogen protection for 13-15 hrs. Next, the reaction temperature was adjusted to 50-60° C. and stirred for 3-5 hrs. The reaction mixture was then concentrated to 275 mL and then DCM (550 mL) was added, followed by water (440 mL). The two phases were separated and the water phase was extracted with DCM (twice with 385 mLs each time). The organic phase was washed with water (twice with 358 mLs each time). Next, the organic phase was concentrated to give 1-tert-butyl 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate 43 g oil. Yield is 71%. ¹H NMR (400 MHz, CDCl₃) δ=7.27-7.29 (m, 4H), 4.46-4.50 (m, 1H), 4.08-4.13 (m, 2H), 4.00-4.02 (m, 1H), 3.59-3.60 (m, 1H), 3.09 (m, 1H), 2.03-2.67 (m, 14H), 0.62-1.42 (m, 57H);

LC/MS: m/z calculated 864.5, found 865.6 (M+1)⁺.

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Step G: Compound 51

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

From the last step, dissolved the 1-tert-butyl 4-((3aR,5aR,
5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)
(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,
8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
[a]chrysen-9-yl) 2,2-dimethylsuccinate (0.8 g, 0.92 mmol) in
3.2 mL DCM, then charged 1.6 mL TFA into the solution.

The reaction mixture was then stirred at 15-25° C. for 1~3
hrs. Next, the reaction was charged with 4 mL DCM and 4 mL
water, stirred well and then allowed to settle. The aqueous
phase was then removed and the organic phase washed two
times with water (4 mLs each). The aqueous phase was then
extracted with DCM (1.6 mL). The combined organic phase

602

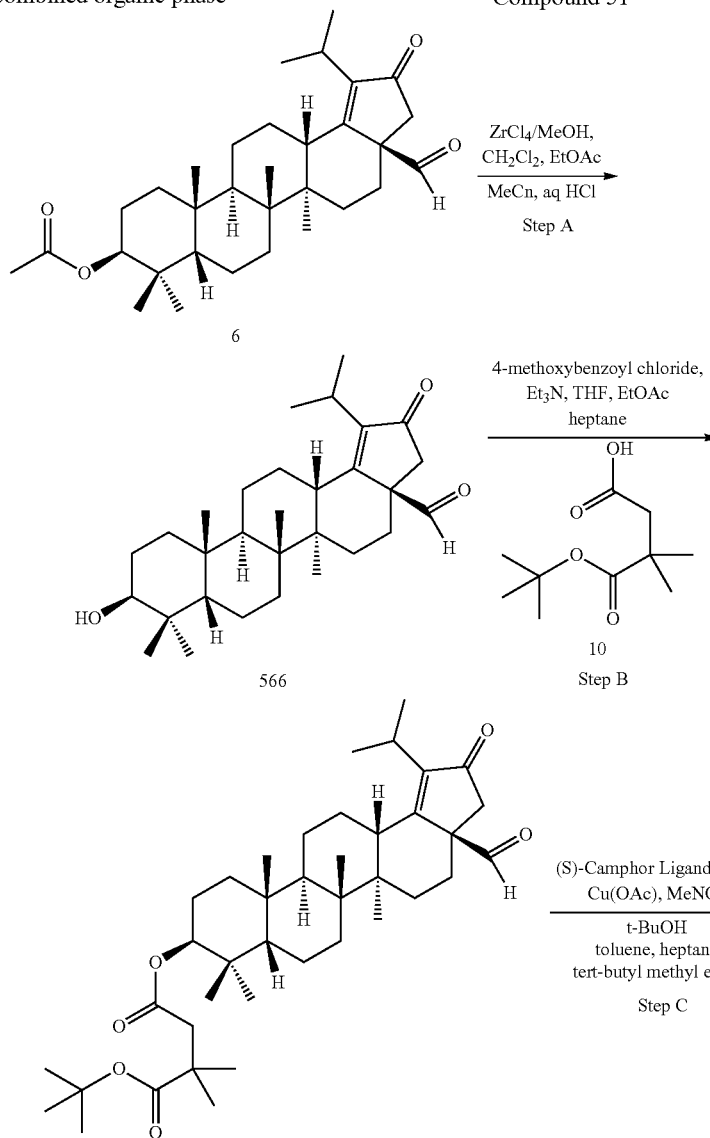
was then washed with saturated sodium bicarbonate until the
pH was between 7-8, followed by two more washes with
water (4 mLs each).

Next, the organic phase was evaporated under vacuum to
give 0.69 g crude product. The crude product was then dis-
solved in 4.8 mL isopropanol and heated to reflux to dissolve
all material. Acetonitrile (19 mL) was added and brought to a
gentle reflux and allowed to start cooling while seeded with 2
mg seed material at 45° C. The mixture was then stirred at 45°
C. for 2 hours. Solids began form and they were cooled to
10~20° C. and stirred for 3 hours. The solution solids were
filtered and then rinsed twice with 1 g acetonitrile each time.

The solids were then dried in a vacuum oven at 45 deg C.
for 18 hours to give the desired product: 4-(((3aR,5aR,5bR,
7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)(2-
(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-
5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (0.59 g,
yield was 78%).

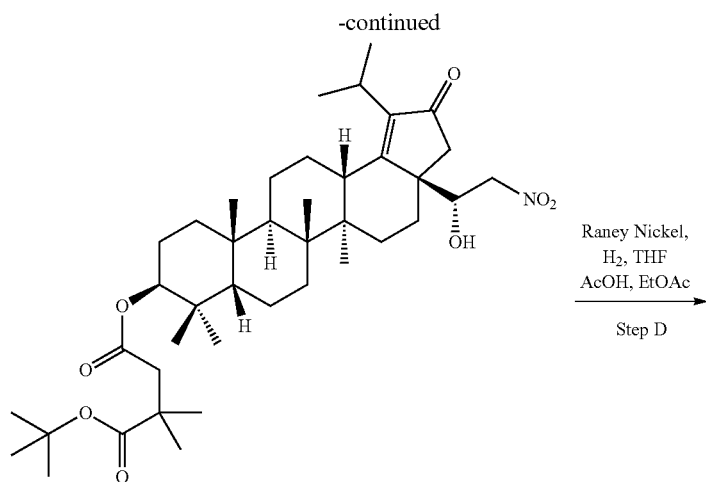
Example 499

Compound 51

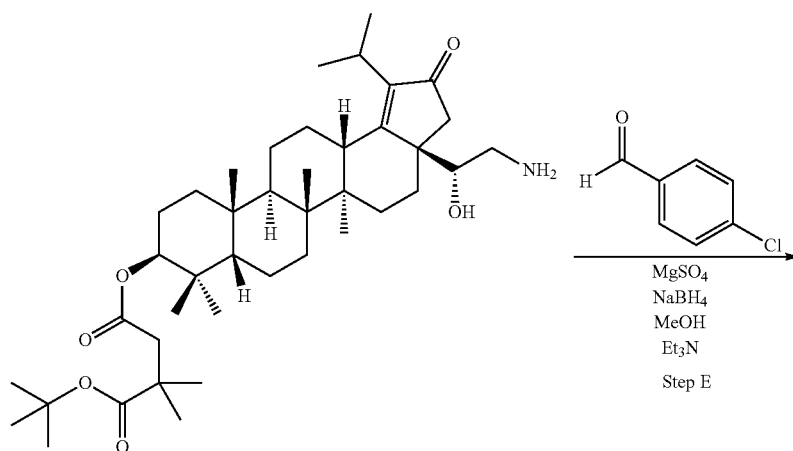


603

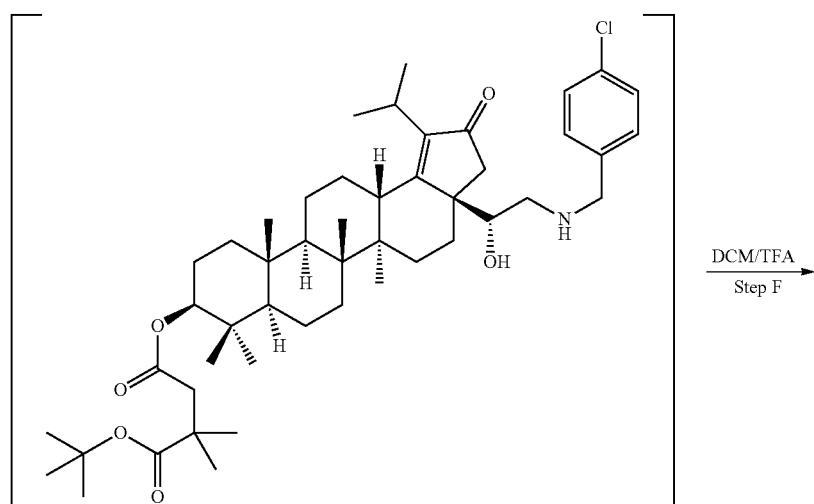
604



569



570

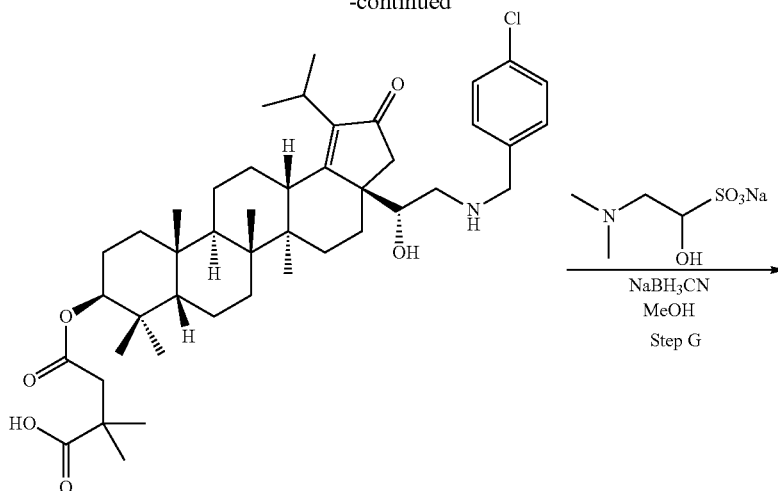


571

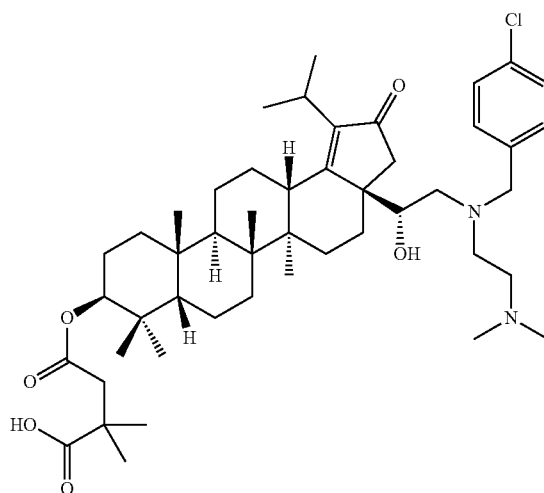
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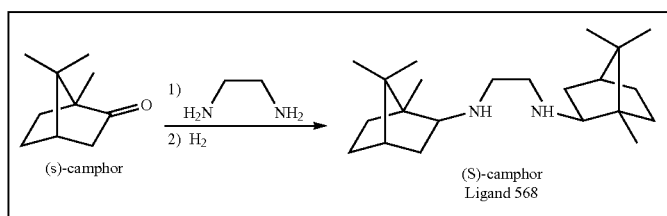
-continued



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Procedures for steps A and D below are not included and are similar to those reported in previous examples and will be understood by one skilled in the art.

Step B: Intermediate 567

1-tert-butyl 4-((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

The starting material (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-9-hydroxy-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-3a-carbaldehyde (5

g, 11 mmol), 4-(tert-butoxy)-3,3-dimethyl-4-oxobutanoic acid (3.4 g, 16.5 mmol), THF ("tetrahydrofuran"-100 mL) and triethylamine (3.4 g, 33 mmol) were charged to a flask.

The mixture was then stirred for 20~30 mins at 0~5° C. Then, 4-methoxybenzoyl chloride (2.8 g, 16.5 mmol) was added through a dropping funnel while the reaction temperature was maintained at 0~5° C. The reaction was then stirred for an additional 1 hour, then DMAP ("dimethylaminopyridine"—0.2 g, 1.65 mmol) was added and the reaction allowed to stir at ambient temperature for approximately 24~30 hours until complete by HPLC.

Next, the reaction was charged with ethyl acetate (100 mL) and water (50 mL), stirred well and allowed to settle. The aqueous phase was removed and the organic phase washed with saturated sodium bicarbonate solution (2x50 mL) followed by water (50 mL). The reaction solution was evaporated under vacuum to approximately 5-10 mL to produce

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solids. An additional amount of heptane (50 mL) was added and the reaction heated back to reflux to nearly form solution and slowly cooled to ambient temperature and let stir for 15 minutes then cooled to 0° C. for approximately two hours and the solids were filtered out. Next, the solids were washed with heptane (2×50 mL) and dried at 50° C. under vacuum to give the desired compound as off-white solid 1-tert-butyl 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-formyl-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate. (4.7 g, yield is 67%).

Step C: Intermediate 569

1-tert-butyl 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

A reaction was charged with 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-formyl-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (6 g, 9.4 mmol), tert-butanol (60 mL) and toluene (18 mL) and temperature was adjusted to 20-25° C. The ligand (N1,N2-bis(1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)ethane-1,2-diamine (0.2 g, 0.57 mmol)) and Copper (I) acetate (0.06 g, 0.47 mmol) were added in a single portion and the reaction allowed to stir at 20-25° C. for 3-5 hrs.

The reaction was then cooled to a temperature of 7-13° C. Afterwards, the reaction was charged with nitromethane (3.9 g, 63 mmol) and allowed to stir at 7-13° C. for approximately 30 hrs. The reaction was charged with additional nitromethane (2.2 g, 35.7 mmol) and allowed to stir at 7-13° C. for approximately 40 hrs. The reaction was charged again with additional nitromethane (2.2 g, 35.7 mmol) and allowed to stir at 7-13° C. for approximately 20 hrs.

Next, the reaction was charged with MTBE ("methyl tertiary butyl ether"—90 mL) and a 15% ammonium chloride solution (36 mL), and allowed to stir for 30 min and then allowed to separate out into two phases. The organic phase was washed with water (30 mL) followed by brine (24 mL). The organic phase was then concentrated to 12 mL and MTBE (3 mL) was added. Next, n-heptane (60 mL) was slowly added and then stirred at 10-20° C. for 2 hrs. The solution was then filtered and washed with n-heptane, the cake was then dried under vacuum at 50-55° C. to give 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate as off-white solid 4.27 g. (65% yield)

Step E: Intermediate 571

1-tert-butyl 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate

4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-amino-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 1-tert-butyl 2,2-dimethylsuccinate (15 g, 22.4 mmol) was placed in a round bottomed flask and then the following were also added: MgSO₄ powder (8.1 g, 56 mmol) and Et₃N (3.6 g, 35.8

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mmol) and p-Chlorobenzaldehyde (5.05 g, 29.1 mmol) and added MeOH (300 mL). The reaction was then allowed to stir for 2 hrs.

The reaction mixture was then cooled to 0 degrees C. on ice-brine bath and treated with solid NaBH₄ (1.61 g, 42.56 mmol) under 10 degrees C. and allowed to stir at 20 degrees for approximately 45 minutes. HPLC after this time showed the reaction was complete. The reaction was then filtered through a Celite™ bed. The solids were rinsed with additional methanol (75 mL) and then dichloromethane (150 mL). The filtrate/rinse was treated with water (150 mL) and shaken in a separation funnel. The organic layers were then washed with water (150 mL). Next, the organic phase was evaporated to give 15 g of 1-tert-butyl 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate as a foamy solid, 84% yield. The crude product was used for the next step directly.

Step F: Compound 46

4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid, 2,2,2-trifluoroacetic acid salt (1:1)

Dissolved 1-tert-butyl 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl) 2,2-dimethylsuccinate (15 g, 18.9 mmol) in dichloromethane (150 mL) and treated with trifluoroacetic acid (30 mL) and allowed to stir at ambient temperature. The reaction was complete in approximately 10 hours. Next, the reaction washed with water (2×150 mL) and the organic phase was evaporated to a minimum volume and ethyl acetate (150 mL vol) was added and then evaporated again to a minimum volume. Evaporated again to a minimum volume and then dissolved in a total of 150 mL volume ethyl acetate.

Next, the resultant solution was heated to near reflux and then diluted with heptane (90 mL) and stirred while cooling to ambient temperature, at which point, solids were formed. The solution was then stirred for 30 minutes and filtered. The filtered solids were rinsed with heptane (30 mL) and dried to give 13 g 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid, 2,2,2-trifluoroacetic acid salt (1:1), 81% yield. ¹HNMR (400 MHz, DMSO-d₆) δ=0.60-1.89 (m, 46H) 2.16-2.19 (d, 1H) 2.32-2.68 (m, 4H) 3.02-3.11 (m, 1H) 4.10-4.26 (m, 3H), 4.38-4.42 (dd, 1H) 5.93 (s, 1H) 7.51 (s, 4H), 8.80-8.98 (d, 2H); LC-MS: m/z calculated (free base) 737.4. found 738.1 (M+1)+.

Step G: Compound 51

4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a, 5b, 8, 8, 11a-pentamethyl-2-oxo-3, 3a, 4, 5, 5a, 5b, 6, 7, 7a, 8, 9, 10, 11, 11a, 11b, 12, 13, 13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

From Step F above, the 4-((3aR, 5aR, 5bR, 7aR, 9S, 11aR, 11bR, 13aS)-3a-((R)-2-((4-chlorobenzyl)amino)-1-hydroxy-

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ethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid trifluoroacetic acid salt (9.0 g, 10.56 mmol) was placed in a round bottomed flask and added dimethylamino acetaldehyde hydrogen sulfite salt (5.05 g, 26.4 mmol) and CH_3COONa (3.46 g, 42.23 mmol) and added MeOH (180 mL) and allowed to stir for 1 hour.

To the reaction mixture was added NaBH_3CN (2.65 g, 42.23 mmol) and allowed to stir at 25 degrees C. for approximately 36 hrs. HPLC after this time showed reaction was complete. Next, the reaction was filtered through a Celite™ bed. The solids were then rinsed with additional methanol (45 mL) and then dichloromethane (90 mL). The filtrate/rinse was treated with water (45 mL) and shaken in separatory funnel. The organic layers were then washed with NaHCO_3 (4 times—45 mL each) and water (two times—45 mL each).

The organic phase was then evaporated to a minimum volume and i-PrOH (36 mL) was added and heated to 75 degrees C. for 2 hours. The resulting solution was then diluted

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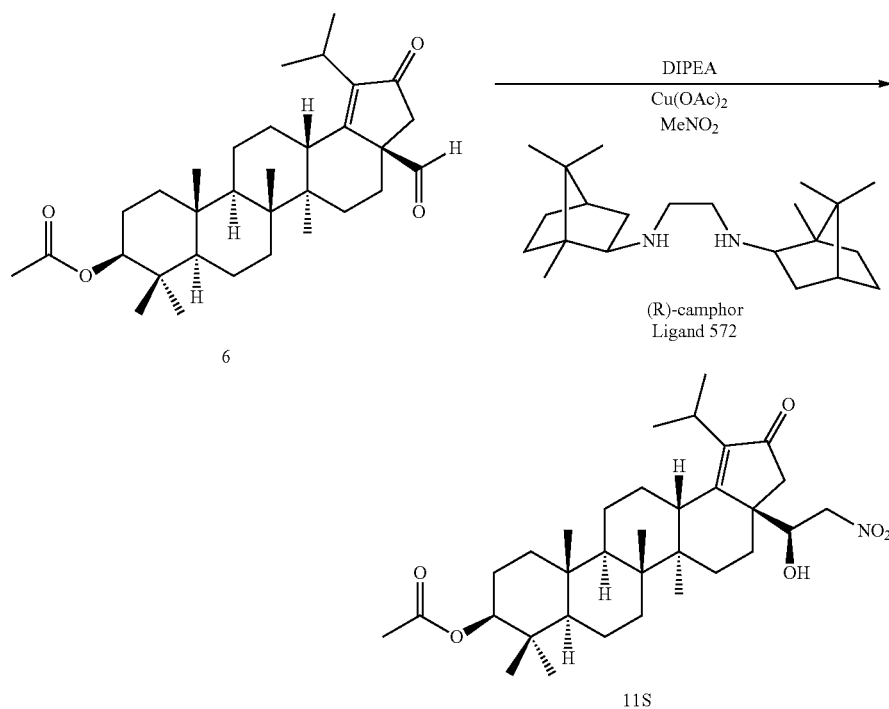
was placed in a round bottomed flask and added i-PrOH (36 mL) and heated to 75 degrees C. for 2 hours. Next, the reaction was diluted with CH_3CN (45 mL) at 75 degrees C. The reaction was then cooled to 5 degrees C. over 4 hours.

The reaction was then stirred at 5 degrees C. for 2 hours and filtered. The filtrate was then rinsed with CH_3CN (9 mL) and dried to give 4.8 g 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid, 84% yield.

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ =0.80-0.29 (m, 14H), 0.97-1.17 (m, 21H), 1.32-1.91 (m, 13), 2.08-2.23 (m, 12H) 2.27-2.38 (m, 3H) 2.40-2.46 (m, 1H) 2.51-2.20 (m, 1H) 2.66-2.70 (m, 1H) 3.00-3.04 (m, 1.0H) 3.71-3.78 (m, 1H) 3.89-3.91 (d, 1H) 4.37-4.41 (dd, 1H), 7.31-7.37 (m, 4H);

LC-MS: m/z calculated 808.5. found 809.1 (M+1)+.

Synthesis of Intermediate 11S



with CH_3CN (45 mL) at 75 degrees C. The solution was then cooled to 5 degrees C. over 4 hours. The solution was then stirred at 5 degrees C. for 2 hours and filtered. The filtrate was then rinsed with CH_3CN (9 mL) and dried to give crude 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (5.6 g, 65% yield).

Re-Crystallization

From Step G above, the crude 4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid (5.6 g)

(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

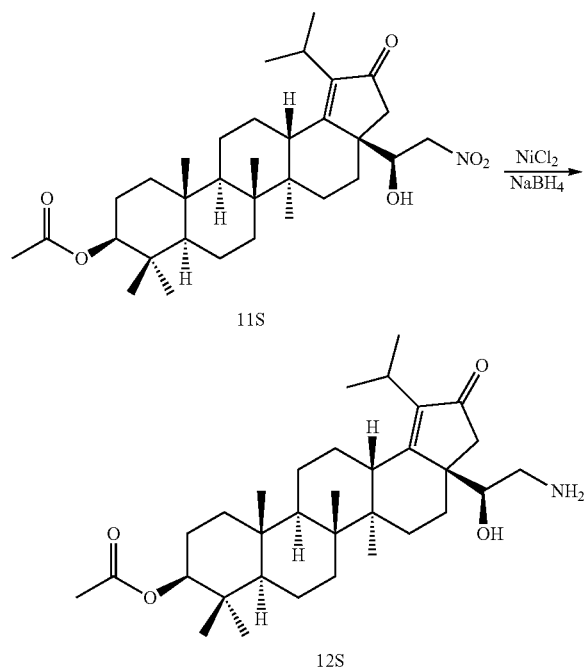
(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-formyl-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (2.0 g, 4.03 mmol) was placed in a flask with n-BuOH (10 mL) and diamine catalyst derived from (R)-camphor (N1,N2-bis(1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)ethane-1,2-diamine, 0.08 g, 0.242 mmol) diamine catalyst and $\text{Cu}(\text{OAc})_2$ (0.037 g, 0.201 mmol) and stirred approximately 16 hours at ambient temperature.

The reaction was then cooled to approximately 0° C. and treated with nitromethane (1.23 g, 20.1 mmol) and Hunig's base ("N,N-diisopropylethylamine"—0.053 g, 0.40 mmol) and allowed to held at 5° C. for 24 hours. Additional BuOH

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(25 ml) and Hunig's base ("N,N-diisopropylethylamine") were added and the reaction held at -10°C . for 24 hours and then at ambient temperature for 24 hours. Solids present in the reaction were filtered to provide the title compound as an off white solid (1.1 g, 49% as ~95:5 mixture of diastereomers). ^1H NMR (500 MHz, CDCl_3) δ =4.89 (bd, 1H), 4.57 (d, 1H), 4.49 (dd, 1H), 4.34 (dd, 1H), 3.21 (m, 1H) 2.94 (dd, 1H) 2.38 (m, 2H) 2.08 to 0.8 (m, 54H) *Note: Integration of the 2.4 to 0.8 region of the spectrum is higher due to the presence of impurities in the sample.

Synthesis of Intermediate 12S



(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-amino-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

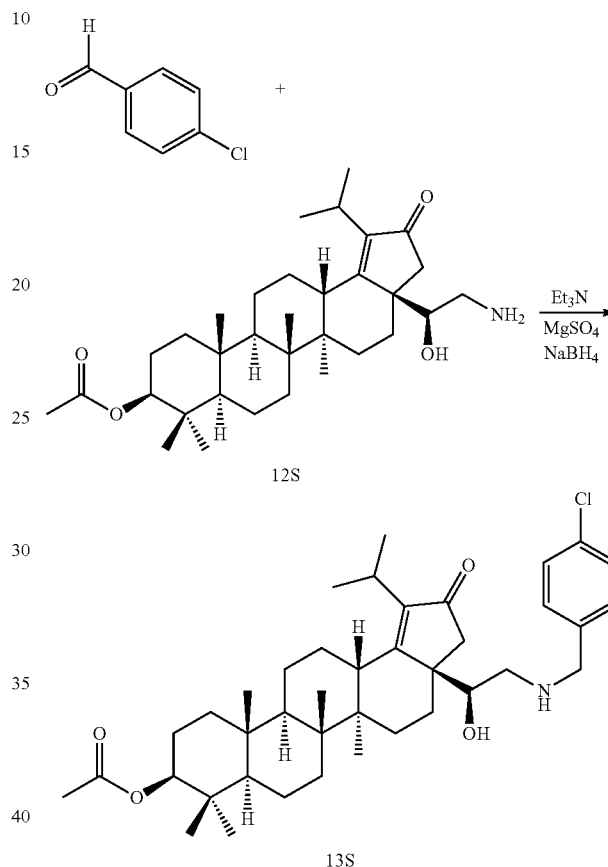
To a flask containing (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-1-hydroxy-2-nitroethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (~95% single diastereomer from the previous Intermediate 11S stage, 0.5 g, 0.89 mmol) in methanol and cooled to -5°C . was added NiCl_2 (0.232 g, 1.79 mmol). The contents were stirred and treated with NaBH_4 (0.475 g, 12.5 mmol), which was added slowly in portions over a 30 minute period while maintaining at approximately -5°C .

An extremely exothermic reaction resulted in some material loss. The reaction was warmed to ambient temperature slowly over a 30 minute period and allowed to stir for approximately 2 hours. The reaction was then quenched with NH_4Cl soln and diluted with methylene chloride. The liquid layers were separated and the organic layer was washed several times with NH_4Cl soln. Next, the organic layer was evaporated to dryness and the residue was chromatographed on silica gel column and eluted with 10% methanol-dichlo-

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romethane. The product containing fractions were evaporated to give title compound as grey solid (250 mg, 53% yield). Sample was carried on to next stage without further characterization.

Synthesis of Intermediate 13S



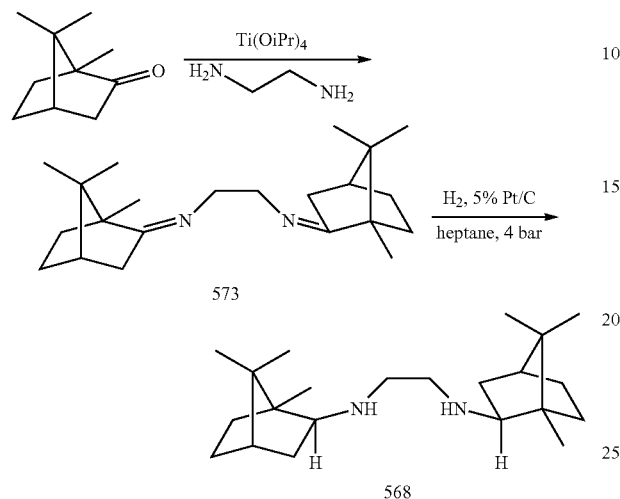
(3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-((4-chlorobenzyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate

To a flask containing (3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((S)-2-amino-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl acetate (200 mg, 379 mmol) and methanol (15 ml) was added triethylamine (15 mg, 0.152 mmol), magnesium sulfate (68 mg, 0.168 mmol) and 4-chlorobenzaldehyde (64 mg, 0.455 mmol). The contents were allowed to stir at ambient temperature for approximately 2 hours. To the resulting mixture was added sodium borohydride (17 mg, 455 mmol) in a single portion and the reaction was allowed to stir at ambient temperature for two and a half days. The reaction was then charged with an additional 20% excess of the p-Cl-benzaldehyde and sodium borohydride and allowed to stir an additional 2 hours. Finally, the reaction was quenched with water, allowed to stir 15 minutes and solids filtered to provide

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title compound contaminated with impurities. LC/MS: m/z calculated 651.4, found 652 (M+1)⁺.

Synthesis of (S) Camphor Derived Chiral Diamine
Ligand 568



Step A: N,N'-bis(isobornyl)ethylenediamine (573)

Titanium (IV) isopropoxide (235.4 g, 830 mmol, 1.04 eq) was added to a flask containing (1S)-(-)-camphor (121.43 g, 798 mmol, 1 eq) at ambient temperature. The reaction was then heated to $\sim 50^\circ\text{C}$. Next, ethylenediamine (31.2 g, 518 mmol, 0.65 eq) was charged to the reaction. The temperature was then kept above 45°C during the addition. The reaction was then heated to $\sim 91^\circ\text{C}$ for 17 hours. Next, the reaction was cooled to $20-25^\circ\text{C}$ and heptane (1.2 L) was added. Water (29.9 g, 1659 mmol, 2.08 eq) was added over at least 15 minutes. The slurry was then stirred for 20 minutes at ambient temperature, cooled to $\sim 0^\circ\text{C}$, and stirred for 30 minutes at $\sim 0^\circ\text{C}$. The slurry was then filtered and the solids washed with heptane (607 mL). The diimine solution was stored $\sim 5^\circ\text{C}$ overnight. The solution was then warmed to ambient temperature and filtered to remove additional salts. Next, the solution was partially concentrated and filtered through CELITE®. Finally, the solution was concentrated to $\sim 608\text{ mL}$ and used as is in the next reaction.

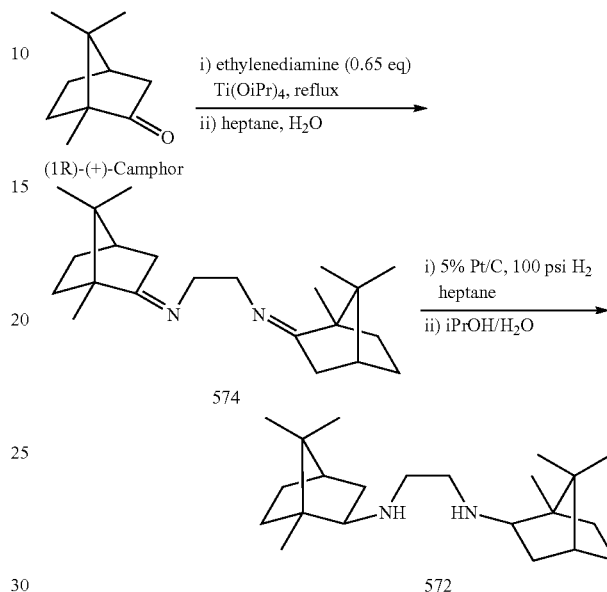
Step B: N,N'-bis(isobornyl)ethylenediamine ligand (568)

To a 1 L Jacketed Lab Reactor (JLR) was added the above diimine solution followed by 5% Pt/C (Johnson-Matthey, B501018-5, 6.6 g). The reaction was hydrogenated for ~ 15 hours at 4 bar at ambient temperature. The reaction was filtered and washed with heptane (300 mL). The solution was concentrated to provide a white solid (115.07 g). This two step procedure was repeated. Both batches were combined. Attempts to crystallize the material from i-PrOH and water failed. The product was extracted with heptane. The heptane layer was then washed with water, brine, dried over sodium sulfate, filtered and concentrated on rotovapor and then high vacuum. The product 568 (222.18 g) was obtained as a white solid and used as is in the asymmetric Henry reaction during the camphor ligand addition step. ^1H NMR (500 MHz, CDCl_3) δ 2.69-2.61 (m, 1H), 2.53-2.47 (m, 2H), 1.71-1.63

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(m, 2H), 1.6-1.43 (m, 3H), 1.1-1.01 (m, 2H), 1.01-0.98 (m, 3H), 0.89-0.83 (m, 3H), 0.81-0.78 (m, 3H)

Synthesis of (R) Camphor Derived Chiral Diamine
Ligand 572



This material was prepared with modifications to methods shown in *Tetrahedron: Asymmetry* 14 (2003) 1451-1454.

Step A: N,N'-bis(isobornyl)ethylenediamine (574)

Titanium isopropoxide (100 mL, 341 mmol, 1.04 eq) was charged to a round bottom flask containing (1R)-(+)-camphor (50 g, 328 mmol) at $20-25^\circ\text{C}$. The reaction mixture was then heated to 50°C , at which time ethylenediamine (14.3 mL, 213 mmol, 0.65 eq) was charged to the reaction. Note: The ethylenediamine addition was exothermic, but it is important to conduct the charge above 45°C to prevent solidification of the reaction mixture as titanium/ethylenediamine complexes are formed. The solution was then heated to reflux ($\sim 90-92^\circ\text{C}$) for 20-24 hours. At that time, the reaction is cooled to $20-25^\circ\text{C}$ and diluted with heptane (500 mL), followed by slow addition of H_2O (12.3 mL, 2.08 eq) over ~ 15 minutes to initiate the formation (and subsequent precipitation) of TiO_2 from the reaction. The slurry was stirred for 20 minutes at $20-25^\circ\text{C}$, cooled to 0°C , and stirred for 20 minutes at 0°C . Finally, the precipitate was filtered and washed with heptane (250 mL) to obtain a solution of diimine (573) in heptane, which was concentrated to 250 mL of heptane (~ 4.6 vol) prior to use in the subsequent hydrogenation stage.

Step B: N,N'-bis(isobornyl)ethylenediamine ligand (572)

Johnson-Matthey Yellow Kit #28 [5% Pt/C, B501018-5] catalyst (2.7 g, 5 wt % wrt 6) was charged to a Parr vessel, followed by a solution of diimine (6) in heptane ($\sim 54\text{ g}$ in 250 mL heptane). The reaction was hydrogenated for 15 h at 100 psi H_2 , 20°C , at which time the only product was observed by LCMS. The mixture was then filtered through a CELITE® pad and washed with heptane (130 mL). The filtrate solvent was swapped from heptanes to isopropanol (270 mL, 5 vol), after which water (86 mL, 1.5 vol) was charged and the

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reaction was heated to reflux to dissolve all material. Slow cooling of the solution to 20° C. resulted in crystallization of the product. Additional water (200 mL, 3.7 vol) was charged over 15 minutes and the reaction was held for an additional 20 minutes. The slurry was then cooled to 0° C. and held for 30 minutes, at which time the product was filtered and washed with a 0° C. mixture of 1:1 water/isopropanol (130 mL) to yield 46.05 g (572) (84.3%) after drying overnight.

The above intermediates 11S,12S, and 13S serve to demonstrate application of the asymmetric Henry reaction in the camphor ligand step to produce the S alcohol on a useful intermediate in consistent yield and selectivity with the earlier examples that provide the R diastereomeric alcohol. It will be apparent to one skilled in the art that this methodology can be employed in combination with the appropriate triterpene derived scaffolds to give either the R or S diastereomer upon choosing the appropriate camphor derived diamine chiral ligand under the conditions outlined herein. Further-

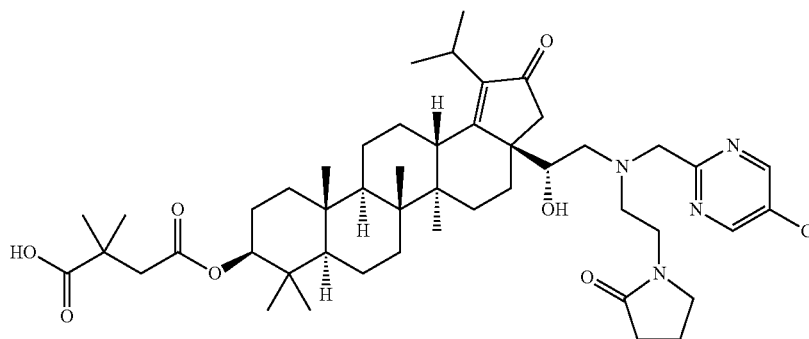
616

more, it is shown that the above nitroalcohol intermediates, whether a mixture of diastereomeric alcohols or in optically enriched form, are useful to provide compounds of Formula I or Formula II.

Example 500

Compound 575

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(((5-chloropyrimidin-2-yl)methyl)(2-(2-oxopyrrolidin-1-yl)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid

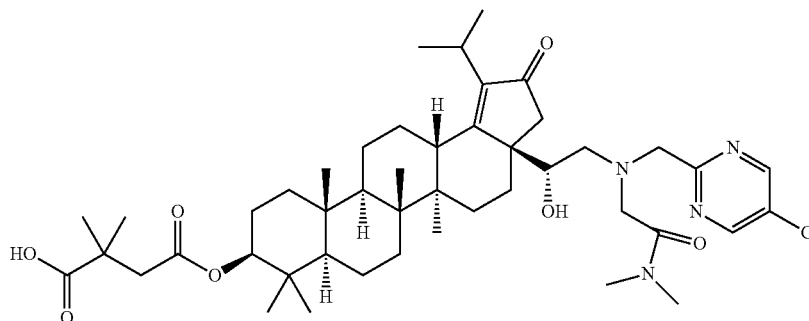


LC/MS: m/z calculated 850.5. found 851.5 (M+1)⁺

Example 501

Compound 576

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-((R)-2-(((5-chloropyrimidin-2-yl)methyl)(2-(dimethylamino)-2-oxoethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-oxobutanoic acid



LC/MS: m/z calculated 824.5. found 825.5 (M+1)⁺

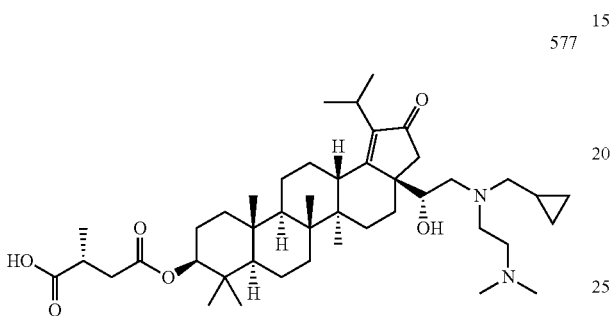
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Example 502

Compound 577

(R)-4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((cyclopropylmethyl)(2-(dimethylamino)
 ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,
 11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,
 11,11a,11b,12,13,13a-octadecahydro-2H-cyclopenta
 [a]chrysen-9-yl)oxy)-2-methyl-4-oxobutanoic acid 5

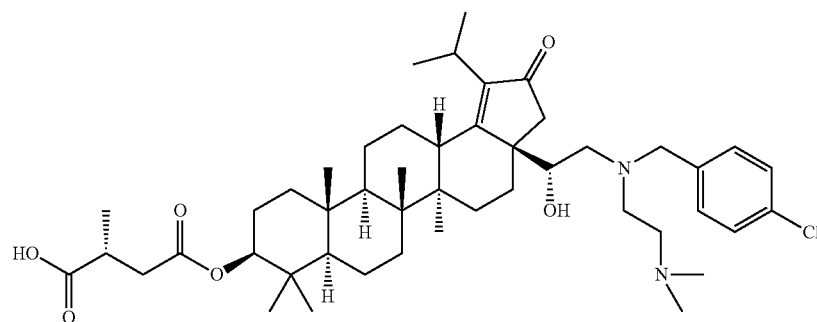


LC/MS: m/z calculated 724.5. found 725.5 (M+1)⁺

Example 503

Compound 578

(R)-4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)
 amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
 pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
 11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
 chrysen-9-yl)oxy)-2-methyl-4-oxobutanoic acid 40

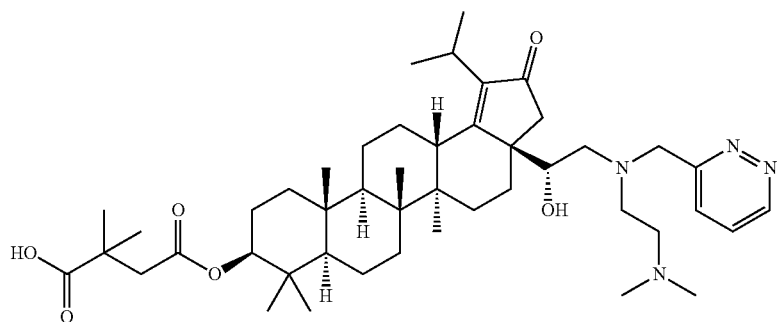


LC/MS: m/z calculated 794.5. found 795.5 (M+1)⁺

Example 504

Compound 579

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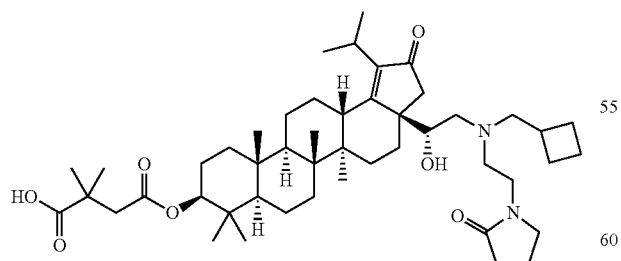
LC/MS: m/z calculated 776.5. found 777.6 (M+1)⁺

Example 505

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Compound 580

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580 50

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LC/MS: m/z calculated 792.6. found 793.6 (M+1)⁺

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Example 506

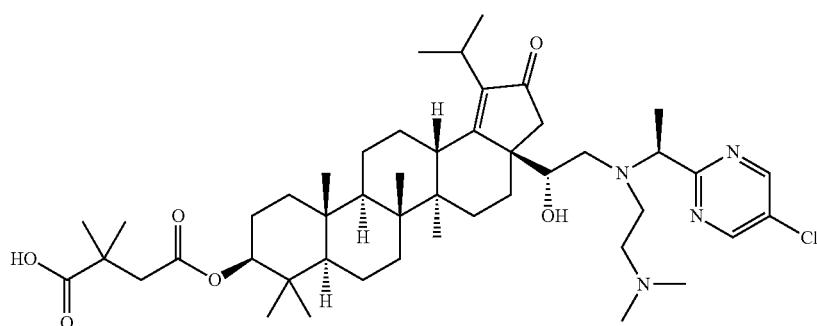
622

Compound 581

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(((S)-1-(5-chloropyrimidin-2-yl)ethyl)(2-
 (dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

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581

LC/MS: m/z calculated 824.5. found 825.5 (M+1)⁺

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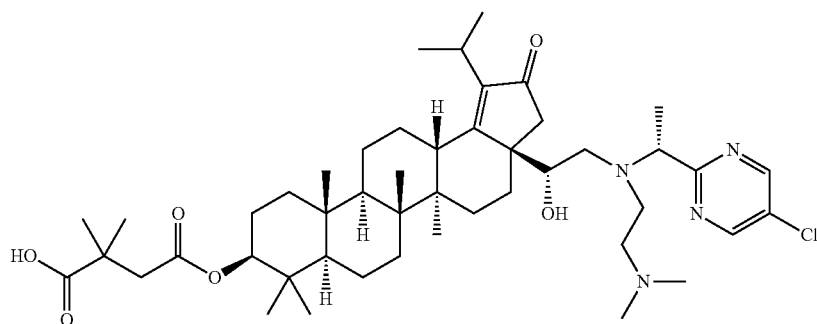
Example 507

Compound 582

4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
 ((R)-2-(((R)-1-(5-chloropyrimidin-2-yl)ethyl)(2-
 (dimethylamino)ethyl)amino)-1-hydroxyethyl)-1-
 isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,
 5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a-
 octadecahydro-2H-cyclopenta[a]chrysen-9-yl)oxy)-
 2,2-dimethyl-4-oxobutanoic acid

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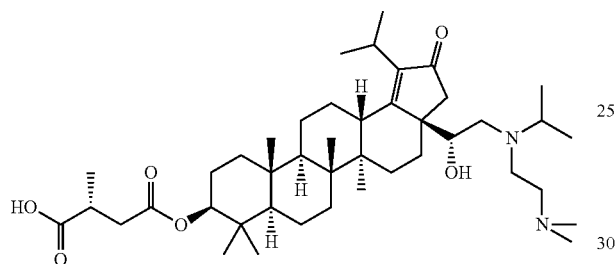
LC/MS: m/z calculated 824.5. found 825.5 (M+1)⁺

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Example 508

Compound 583

(R)-4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((2-(dimethylamino)ethyl)(isopropyl)amino)-
1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,
12,13,13a-octadecahydro-2H-cyclopenta[a]chrysen-
9-yl)oxy)-2-methyl-4-oxobutanoic acid



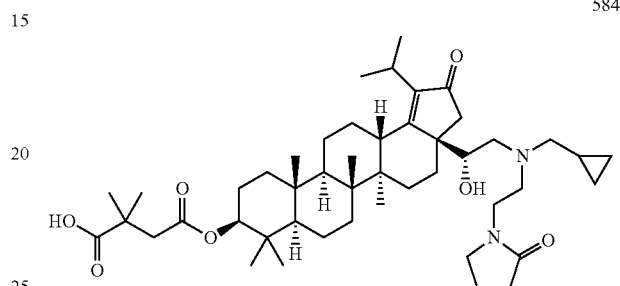
Exact Mass: 712.54

LC/MS: m/z calculated 712.5. found 713.7 (M+1)⁺**624**

Example 509

Compound 584

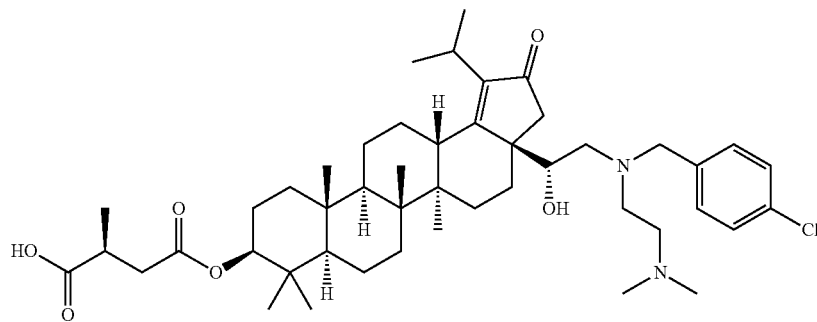
4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((cyclopropylmethyl)(2-(2-oxopyrrolidin-1-
yl)ethyl)amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,
8,8,11a-pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,
10,11,11a,11b,12,13,13a-octadecahydro-2H-
cyclopenta[a]chrysen-9-yl)oxy)-2,2-dimethyl-4-
oxobutanoic acid

LC/MS: m/z calculated 778.6. found 779.6 (M+1)⁺

Example 510

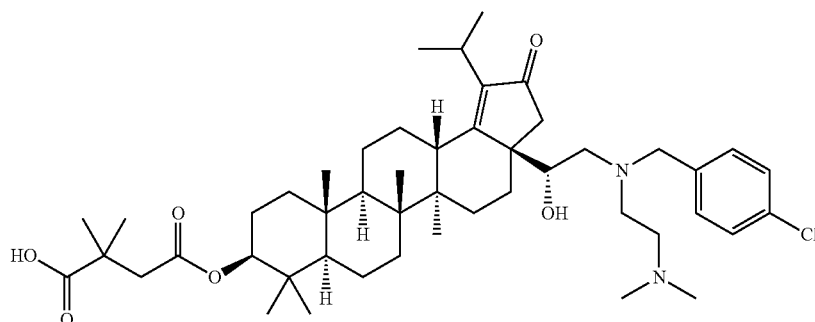
Compound 585

(S)-4-(((3aR,5aR,5bR,7aR,9S,11aR,11bR,13aS)-3a-
((R)-2-((4-chlorobenzyl)(2-(dimethylamino)ethyl)
amino)-1-hydroxyethyl)-1-isopropyl-5a,5b,8,8,11a-
pentamethyl-2-oxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,
11a,11b,12,13,13a-octadecahydro-2H-cyclopenta[a]
chrysen-9-yl)oxy)-2-methyl-4-oxobutanoic acid

LC/MS: m/z calculated 794.5. found 795.5 (M+1)⁺

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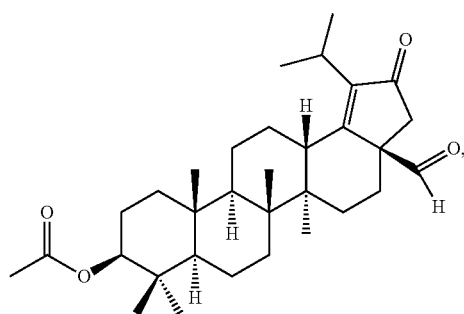
After the above description of synthesis procedures for the compounds described herein, there is provided in accordance with other embodiments of the present invention, a process for preparing a compound of Formula (I) having the structure:



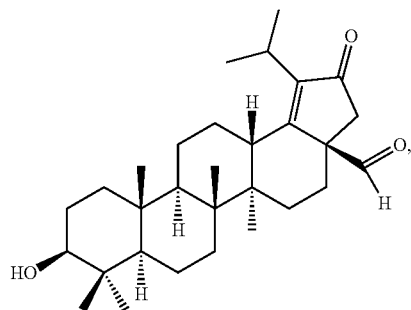
626

comprising the steps of:

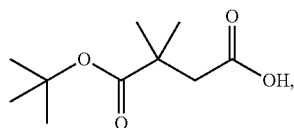
(1) saponifying a compound having the structure:



in the presence of a first metal catalyst, in order to provide a compound having the structure:



(2) reacting the compound product of Step (1), with a compound having the structure:



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in the presence of an acid chloride and a tertiary amine in order to provide a compound having the structure:

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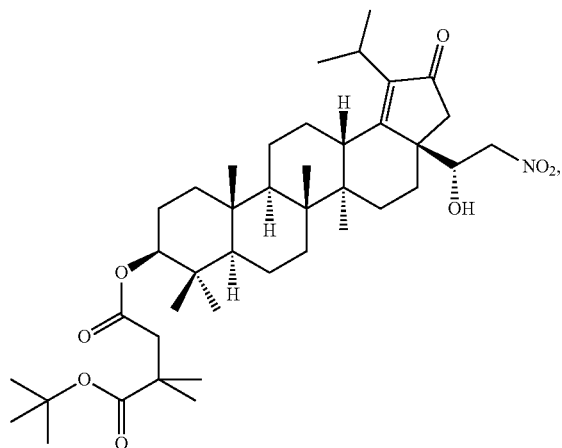
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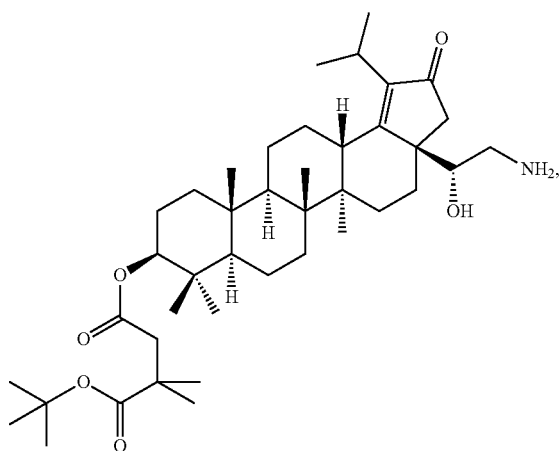
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(3) reacting nitromethane with the compound product of Step (2) in the presence of a chiral ligand, an optional base, and a second metal catalyst in order to provide a compound having the structure:

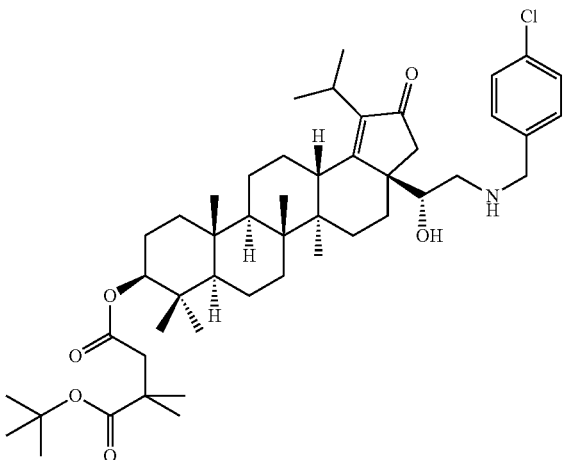


(4) reducing the compound product of Step (3), in the presence of a third metal catalyst and hydrogen gas in order to provide a compound having the structure:

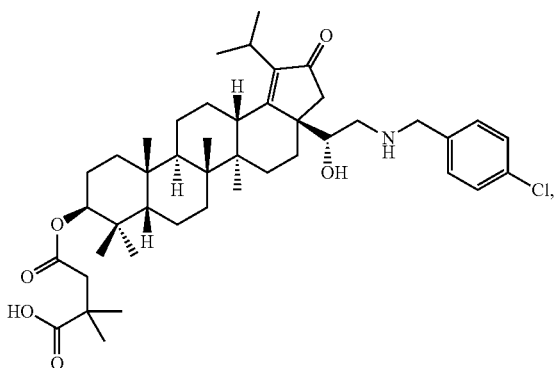
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(5) reacting p-chlorobenzaldehyde with the compound product of Step (4), in the presence of a metal hydride, to provide a compound having the structure:

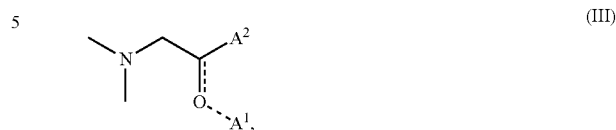


(6) acidifying the compound product of Step (5), in the presence of an acid in order to provide the compound having the structure:

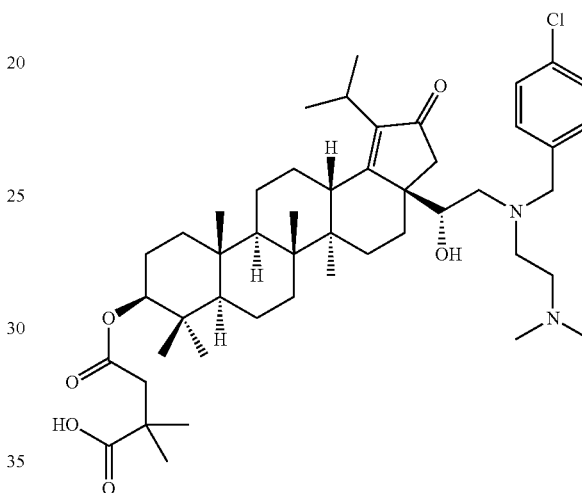


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(7) reacting the compound product of Step (6) with a compound having the structure according to Formula III:



wherein A^1 is either optionally absent or is selected from the group consisting —H, methyl, and ethyl; and A^2 is selected from the group consisting of —H, hydroxyl, methoxy, ethoxy, and $-\text{SO}_3^-\text{Na}^+$; while in the presence of a metal hydride in order to provide the compound having the structure:



As will be known to one of skill in the art after reading the synthetic procedures described here and the process steps described above and below, several suitable chemical components can be used to carry out the process steps. Such suitable chemical components can be used interchangeably with any process step description described herein according to knowledge in the art.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein one or more of Steps (1)-(7) are conducted in the presence of a solvent.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein one or more of Steps (1)-(7) are conducted in the presence of an organic solvent.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein one or more of Steps (1)-(7) are conducted in the presence of a solvent that is selected from the group consisting of water, dichloromethyl, methanol, tetrahydrofuran, tetrahydrofuran acetate, ethanol, ethyl acetate, heptane, isopropanol, tert-butanol, toluene, acetonitrile, and tert-butyl methyl ether.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the first metal catalyst of Step (1) is a metal halide.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the first metal catalyst of Step (1) is zirconium tetrachloride.

In accordance with other embodiments of the present invention, there is provided a process for preparing a com-

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pound of Formula (I), wherein the acid chloride of Step (2) is selected from the group consisting of benzoyl chloride and methoxybenzoyl chloride.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the acid chloride of Step (2) is methoxybenzoyl chloride.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the tertiary amine of Step (2) is a tertiary amine coupling agent.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the tertiary amine of Step (2) is selected from the group consisting of triethylamine, N,N-diisopropylethylamine, and 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the tertiary amine of Step (2) is 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the tertiary amine of Step (2) is triethylamine.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the second metal catalyst of Step (3) is a compound comprising a metal selected from the group consisting of Zn, Co, Cu, Mg, and Cr.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the second metal catalyst of Step (3) is a compound comprising a metal selected from the group consisting of Cu(I) and Cu(II).

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the second metal catalyst of Step (3) is a compound comprising Cu(I).

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the second metal catalyst of Step (3) is selected from the group consisting of Copper(I) acetate and Cu(II) acetate.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the second metal catalyst of Step (3) is Copper(I) acetate.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the second metal catalyst of Step (3) is Copper(II) acetate.

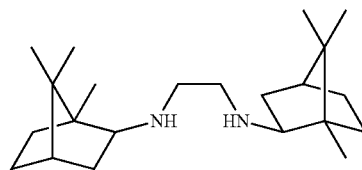
In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the optional base of Step (3) is selected from the group consisting of alkali metal hydroxides, alkoxides, carbonates, fluoride anions, and nonionic organic amine bases.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the optional base of Step (3) is $^t\text{Pr}_2\text{Net}$.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the chiral ligand of Step (3) is a derivative of S-Camphor.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the chiral ligand of Step (3) is a compound having the structure:

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In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the third metal catalyst of Step (4) is selected from the group consisting of Raney Nickel, nickel, nickel chloride, aluminum, palladium, copper, zinc, chromium, iridium, rhodium, platinum, and combinations thereof.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the third metal catalyst of Step (4) is Raney Nickel.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the hydrogen of Step (4) is hydrogen gas.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the metal hydride of Step (5) is a borohydride.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the metal hydride of Step (5) is selected from the group consisting of NaBH_4 and $\text{NaBH}(\text{OAc})_3$.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the metal hydride of Step (5) is NaBH_4 .

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the metal hydride of Step (5) is $\text{NaBH}(\text{OAc})_3$.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the acid of Step (6) is selected from the group consisting of trifluoroacetic acid, HCl, and trichloroacetic acid.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the acid of Step (6) is trifluoroacetic acid.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the A^2 of Step (7) is $-\text{SO}_3\text{Na}$.

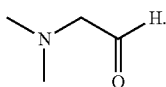
In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the A^2 of Step (7) is $-\text{H}$.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the A^1 of Step (7) is absent.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the A^1 of Step (7) is $-\text{H}$.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the compound of Formula III of Step (7) has the following structure:

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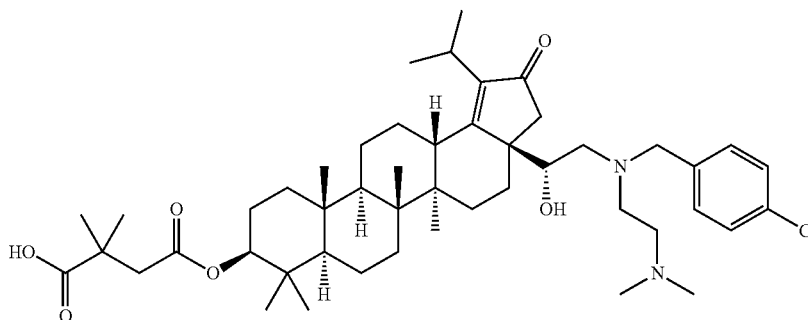


In accordance with other embodiments of the present invention, there is provided a process for preparing a com-

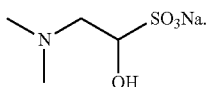
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In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the metal hydride of Step (7) is NaBH_3CN .

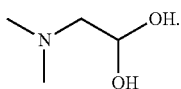
In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I) having the structure:



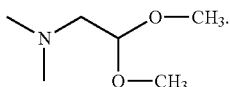
compound of Formula (I), wherein the compound of Formula III of Step (7) has the following structure:



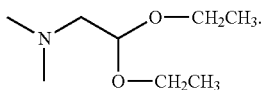
In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the compound of Formula III of Step (7) has the following structure:



In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the compound of Formula III of Step (7) has the following structure:

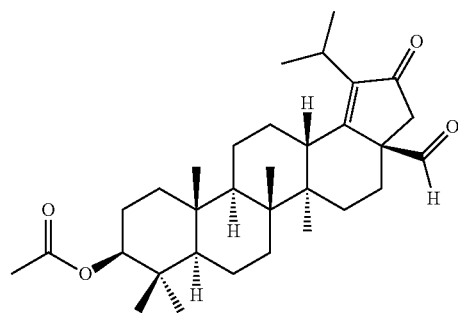


In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the compound of Formula III of Step (7) has the following structure:

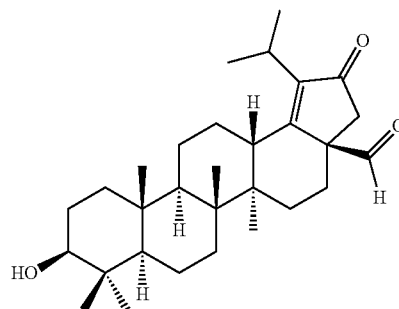


In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the metal hydride of Step (7) is a borohydride.

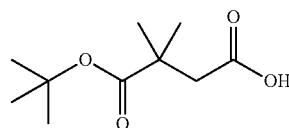
comprising the steps of:
(1) saponifying a compound having the structure:



in the presence of a first metal catalyst, in order to provide a compound having the structure:

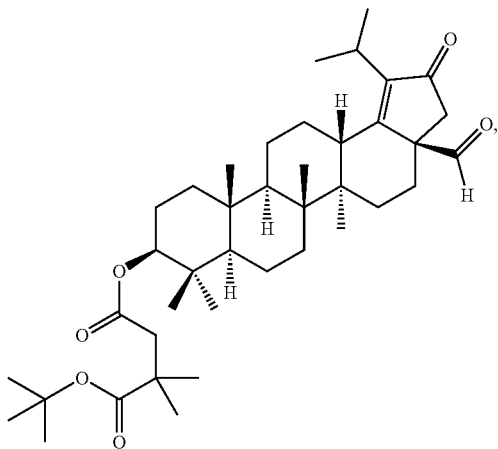


(2) reacting the compound product of Step (1), with a compound having the structure:

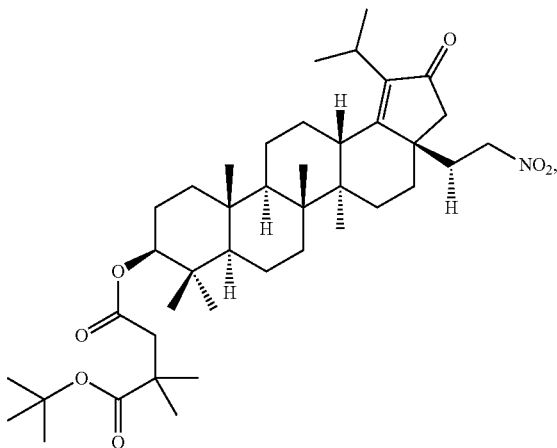


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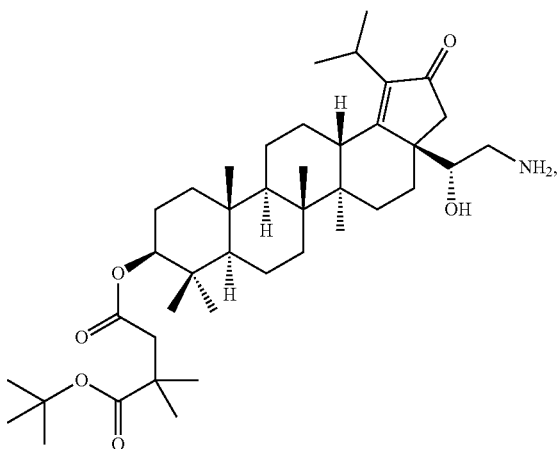
in the presence of an acid chloride and a tertiary amine in order to provide a compound having the structure:



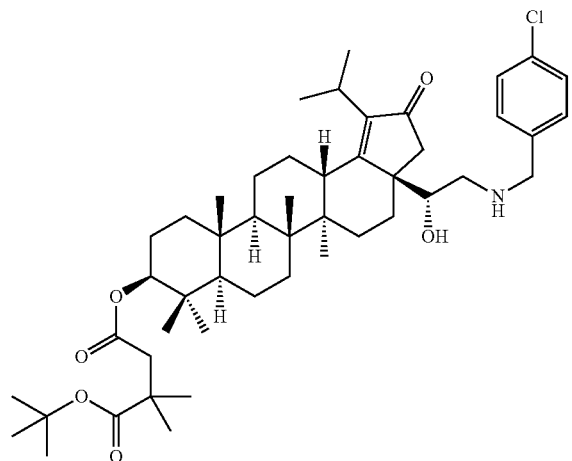
(3) reacting nitromethane with the compound product of Step (2) in the presence of a chiral ligand and a base and a second metal catalyst in order to provide a compound having the structure:



(4) reducing the compound product of Step (3), in the presence of a third metal catalyst and hydrogen gas in order to provide a compound having the structure:

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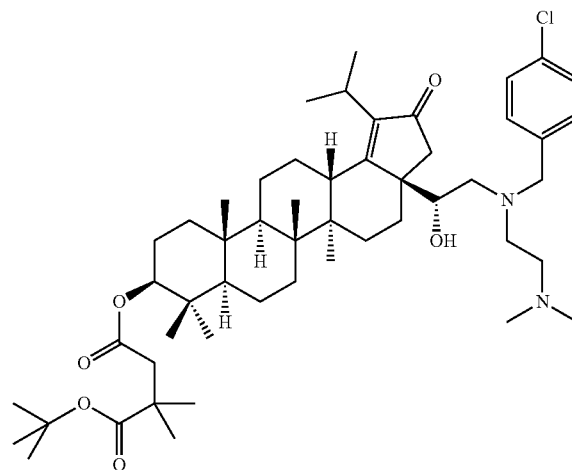
(5) reacting p-chlorobenzaldehyde with the compound product of Step (4), in the presence of a metal hydride and a tertiary amine, to provide a compound having the structure:



(6) reacting the compound product of Step (5) with a compound having the structure according to Formula III:

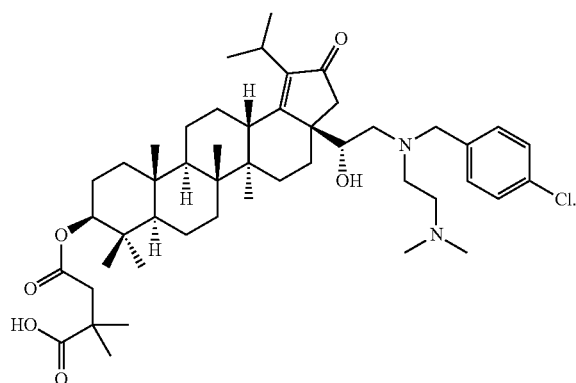


wherein A^1 is either optionally absent or is selected from the group consisting —H, methyl, and ethyl; and A^2 is selected from the group consisting of —H, methoxy, ethoxy, hydroxyl, and $-\text{SO}_3^-\text{Na}^+$; while in the presence of a metal hydride in order to provide the compound having the structure:



(7) acidifying the compound product of Step (6), in the presence of an acid in order to provide the compound having the structure:

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With regards to the synthesis procedures herein, and in accordance with other embodiments of the present invention,

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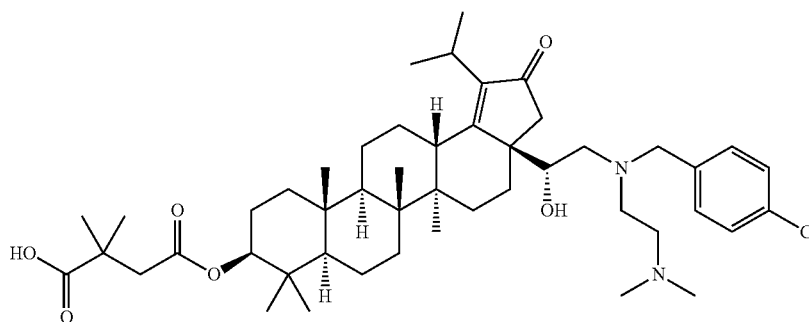
In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the metal hydride of Step (5) is a borohydride.

5 In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the metal hydride of Step (5) is selected from the group consisting of NaBH_4 and $\text{NaBH}(\text{OAc})_3$.

10 In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the metal hydride of Step (5) is NaBH_4 .

15 In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the tertiary amine of Step (6) is triethylamine.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), having the structure:



there is also provided a process for preparing a compound of Formula (I), wherein one or more of Steps (1)-(7) are conducted in the presence of a solvent.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein one or more of Steps (1)-(7) are conducted in the presence of an organic solvent.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein one or more of Steps (1)-(7) are conducted in the presence of a solvent that is selected from the group consisting of water, dichloromethyl, methanol, tetrahydrofuran, tetrahydrofuran acetate, ethanol, ethyl acetate, heptane, isopropanol, tert-butanol, toluene, acetonitrile, and tert-butyl methyl ether.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the base of Step (3) is selected from the group consisting of alkali metal hydroxides, alkoxides, carbonates, fluoride anions, and nonionic organic amine bases.

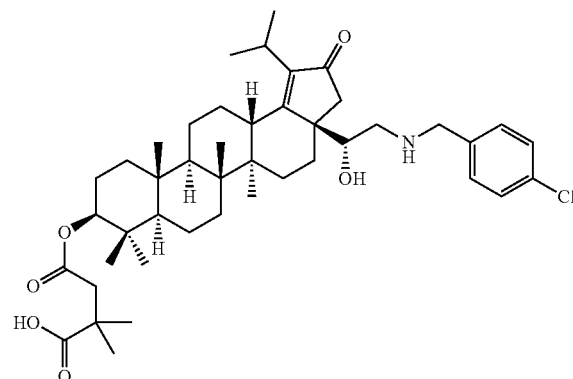
In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the base of Step (3) is $^t\text{Pr}_2\text{Net}$.

In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the tertiary amine of Step (5) is selected from the group consisting of triethylamine and 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride.

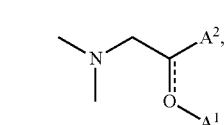
In accordance with other embodiments of the present invention, there is provided a process for preparing a compound of Formula (I), wherein the tertiary amine of Step (5) is triethylamine.

comprising the steps of:

(1) reacting a compound having the structure:



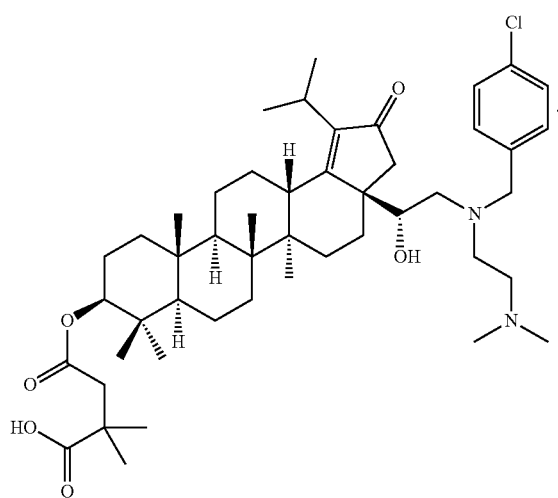
with a compound having the structure according to Formula III:



wherein A^1 is either optionally absent or is selected from the group consisting $-\text{H}$, methyl, and ethyl; and A^2 is selected

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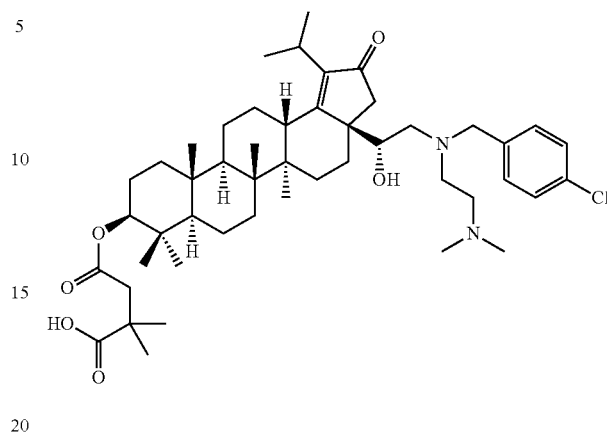
from the group consisting of —H, methoxy, ethoxy, hydroxyl, and —SO₃[−]Na⁺; while in the presence of a metal hydride in order to provide the compound having the structure:



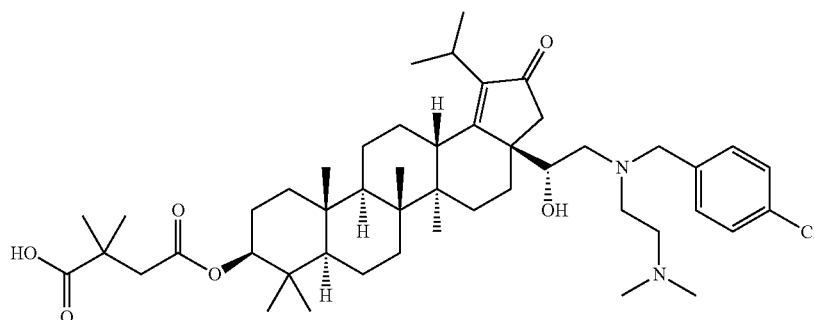
In accordance with other embodiments of the present invention and the suitable process step components recited above, there is provided a process for preparing a compound of Formula (I), having the structure:

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in the presence of an acid in order to provide the compound having the structure:

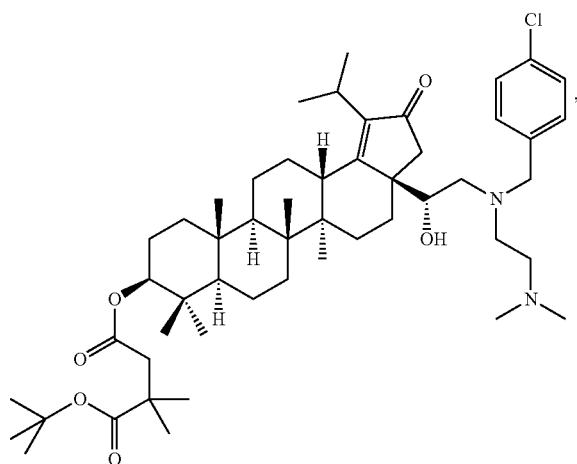


In accordance with other embodiments of the present invention and the suitable process step components recited above, there is provided a process for preparing a compound of Formula (I), having the structure:



comprising the steps of:

(1) acidifying a compound having the structure:



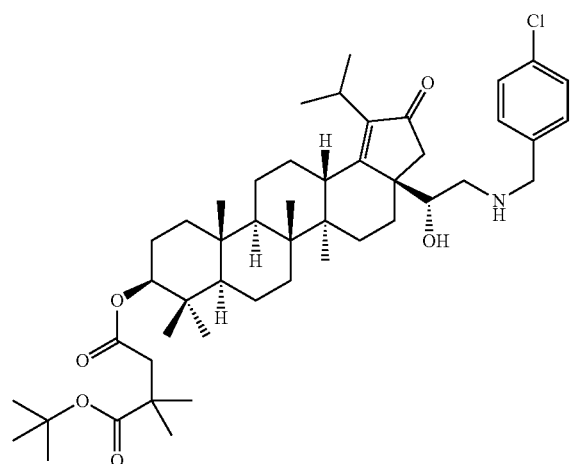
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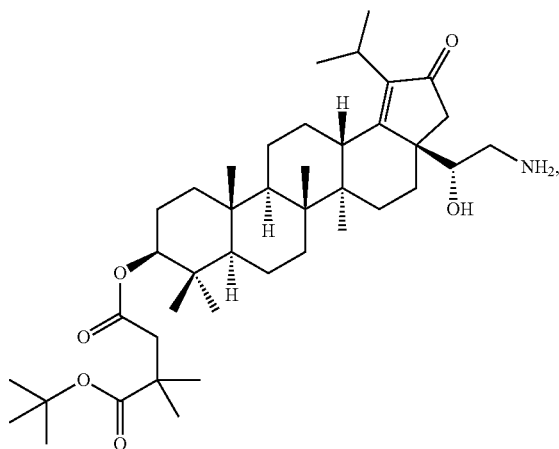
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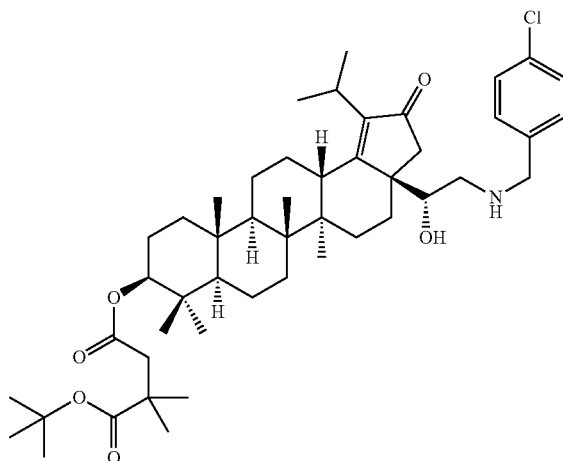
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comprising the steps of:

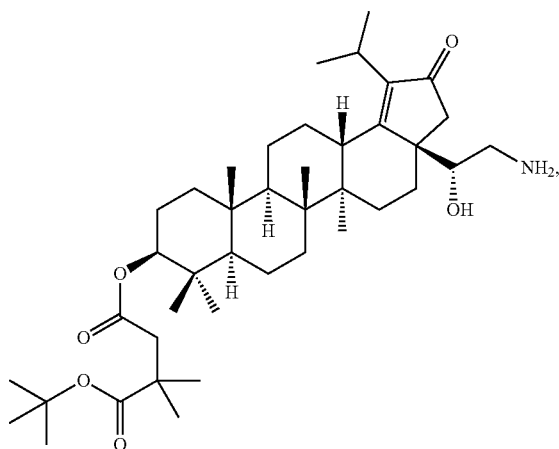
- (1) reacting p-chlorobenzaldehyde with a compound having the structure:



in the presence of a metal hydride to provide the compound having the structure:



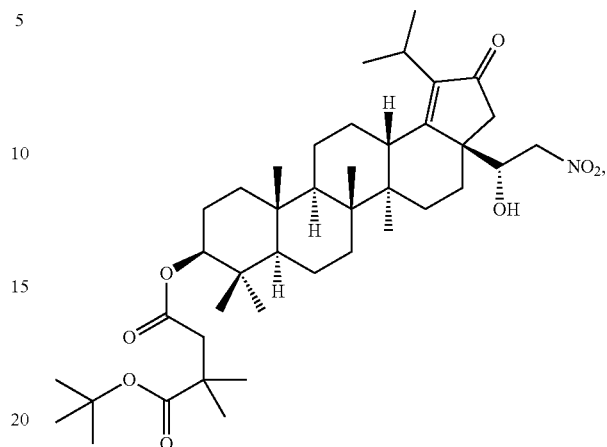
In accordance with other embodiments of the present invention and the suitable process step components recited above, there is provided a process for preparing a compound of Formula (I), having the structure:



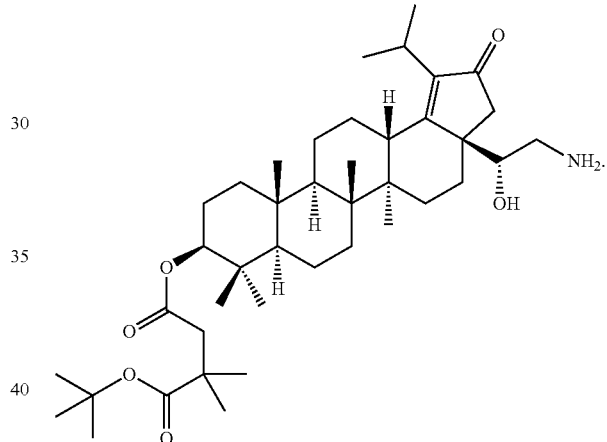
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comprising the steps of:

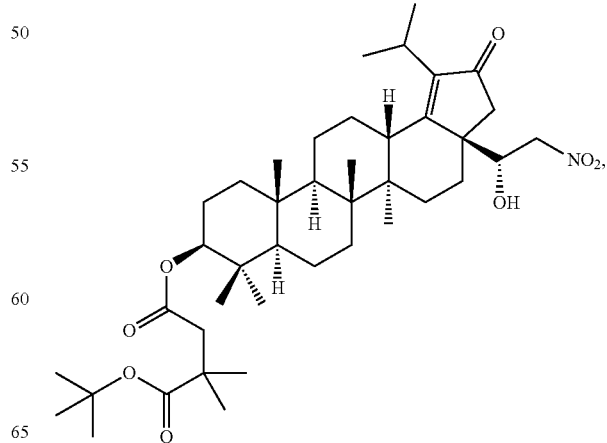
- (1) reducing a compound having the structure:



in the presence of a metal catalyst and hydrogen gas in order to provide the compound having the structure:



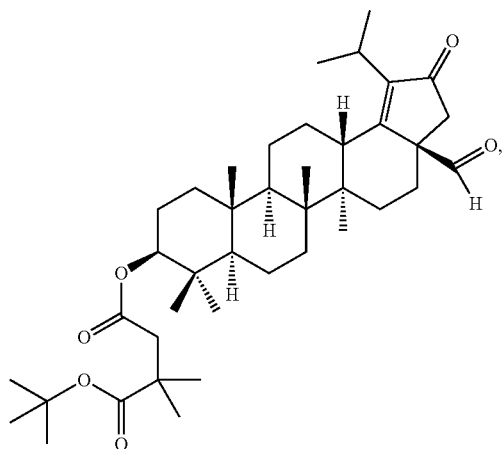
In accordance with other embodiments of the present invention and the suitable process step components recited above, there is provided a process for preparing a compound of Formula (I), having the structure:



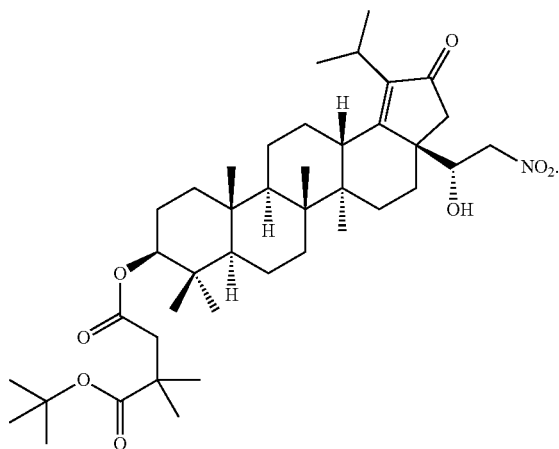
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comprising the steps of:

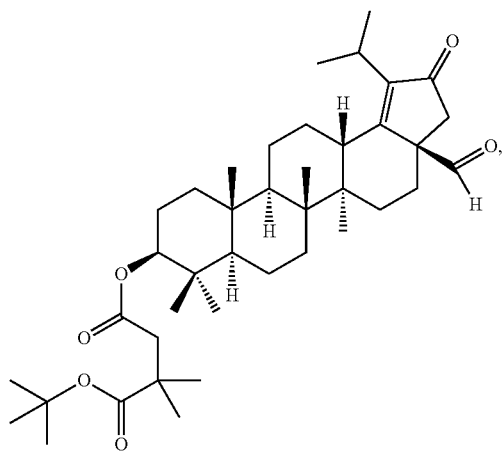
- (1) reacting nitromethane with a compound having the structure:



in the presence of a chiral ligand and a metal catalyst in order to provide a compound having the structure:

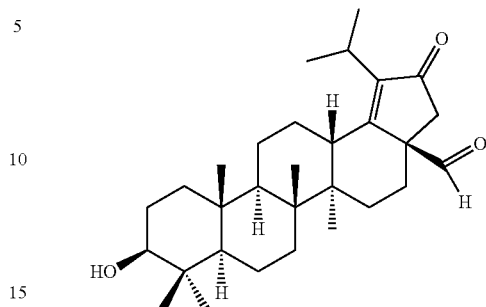


In accordance with other embodiments of the present invention and the suitable process step components recited above, there is provided a process for preparing a compound of Formula (I), having the structure:

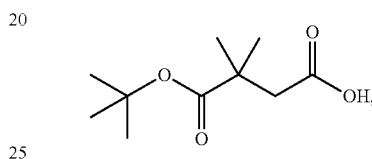
**642**

comprising the steps of:

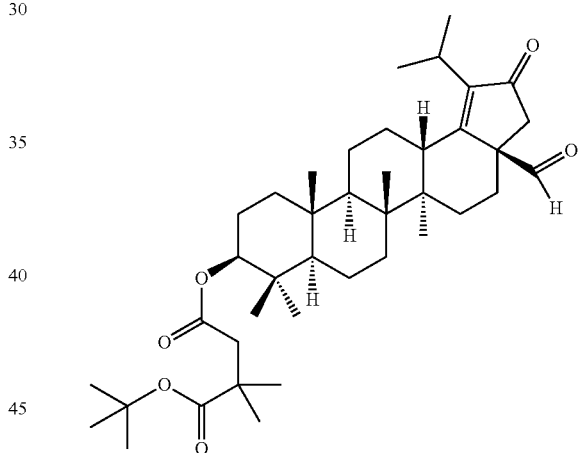
- (1) reacting a compound having the structure:



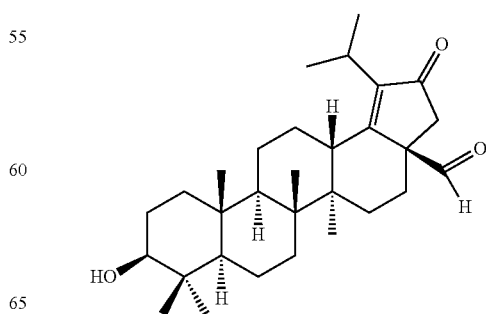
with a compound having the structure:



in the presence of an acid chloride and a tertiary amine in order to provide the compound having the structure:



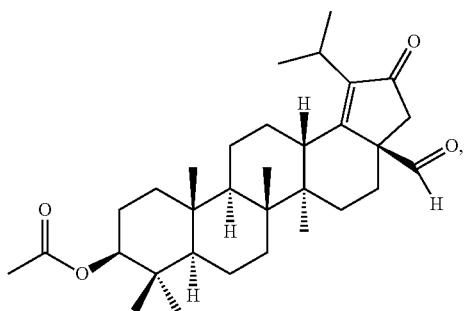
In accordance with other embodiments of the present invention and the suitable process step components recited above, there is provided a process for preparing a compound of Formula (I), having the structure:



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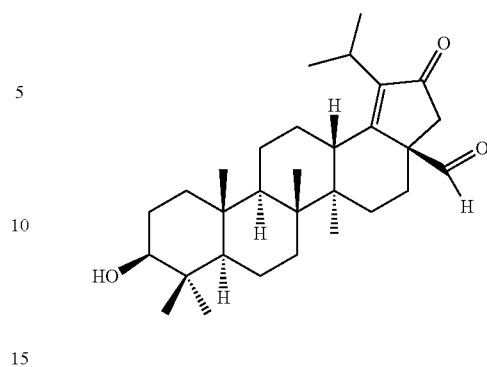
comprising the steps of:

(1) saponifying a compound having the structure:

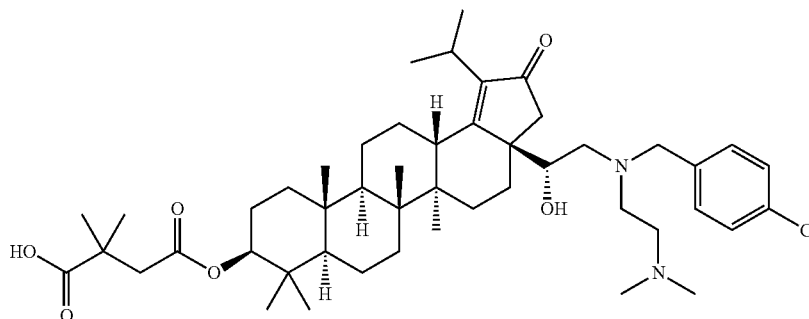


in the presence of a metal catalyst, in order to provide the compound having the structure:

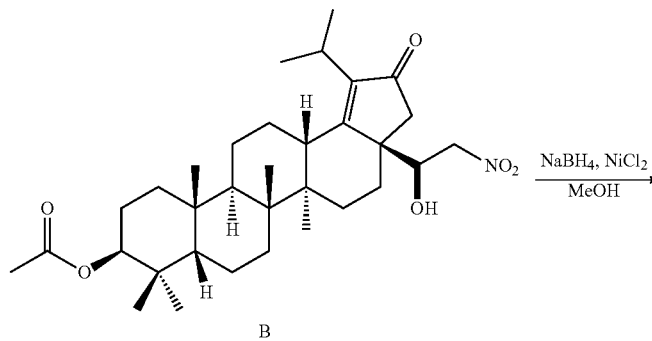
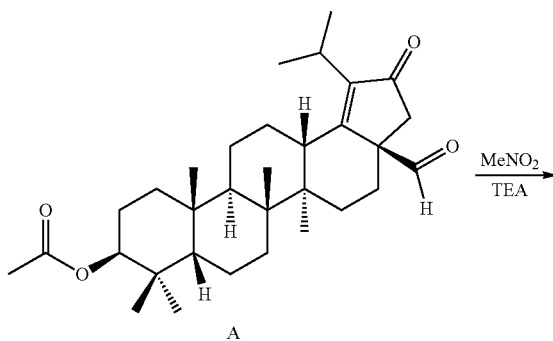
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In accordance with other embodiments of the present invention and the suitable process step components recited above, there is provided a process for preparing a compound of Formula (I), having the structure:



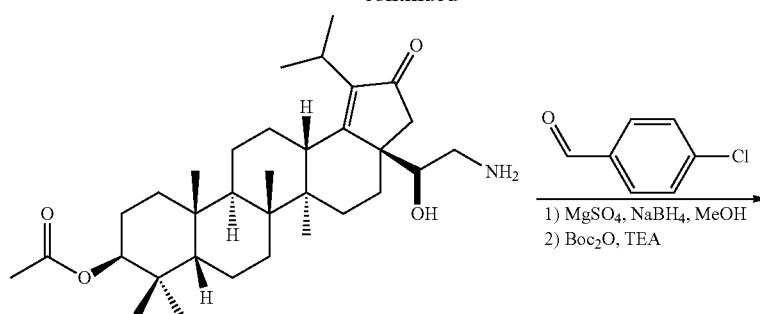
comprising the steps according to the following synthesis scheme. As will be known to one of skill in the art, the above reagents recited in still other synthesis schemes may be substituted within the synthesis scheme below as described above.



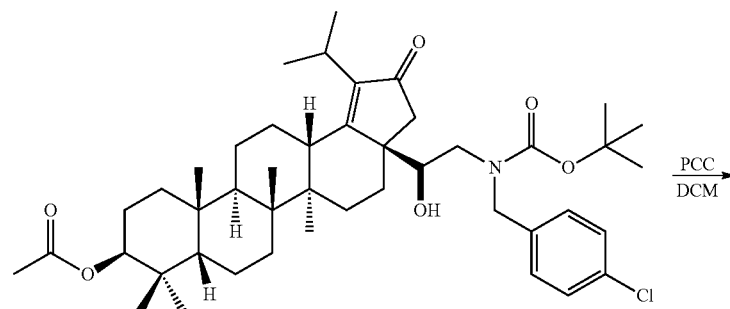
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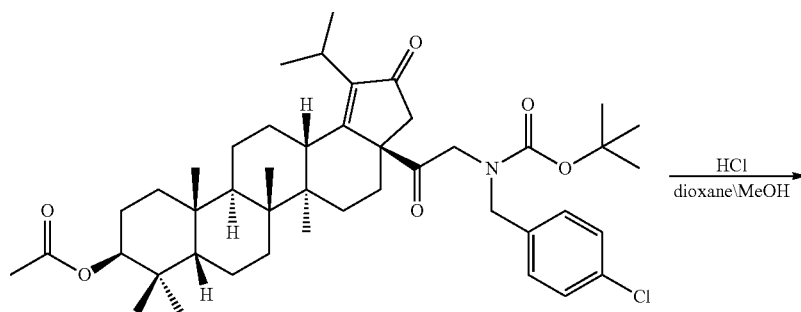
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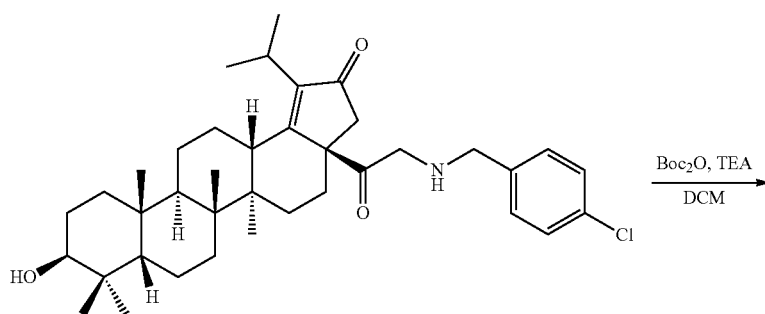
C



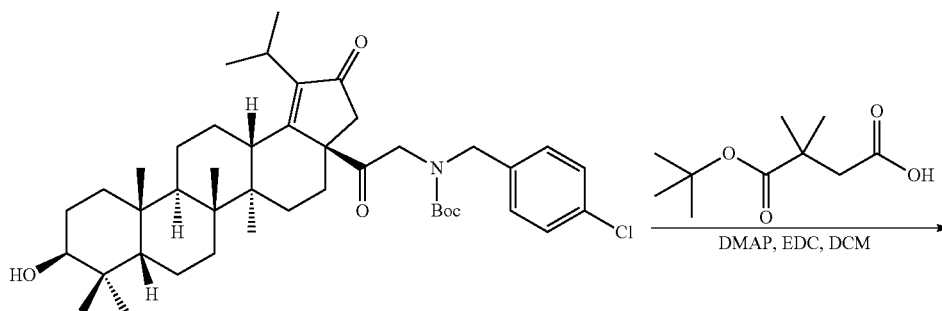
D



E



F

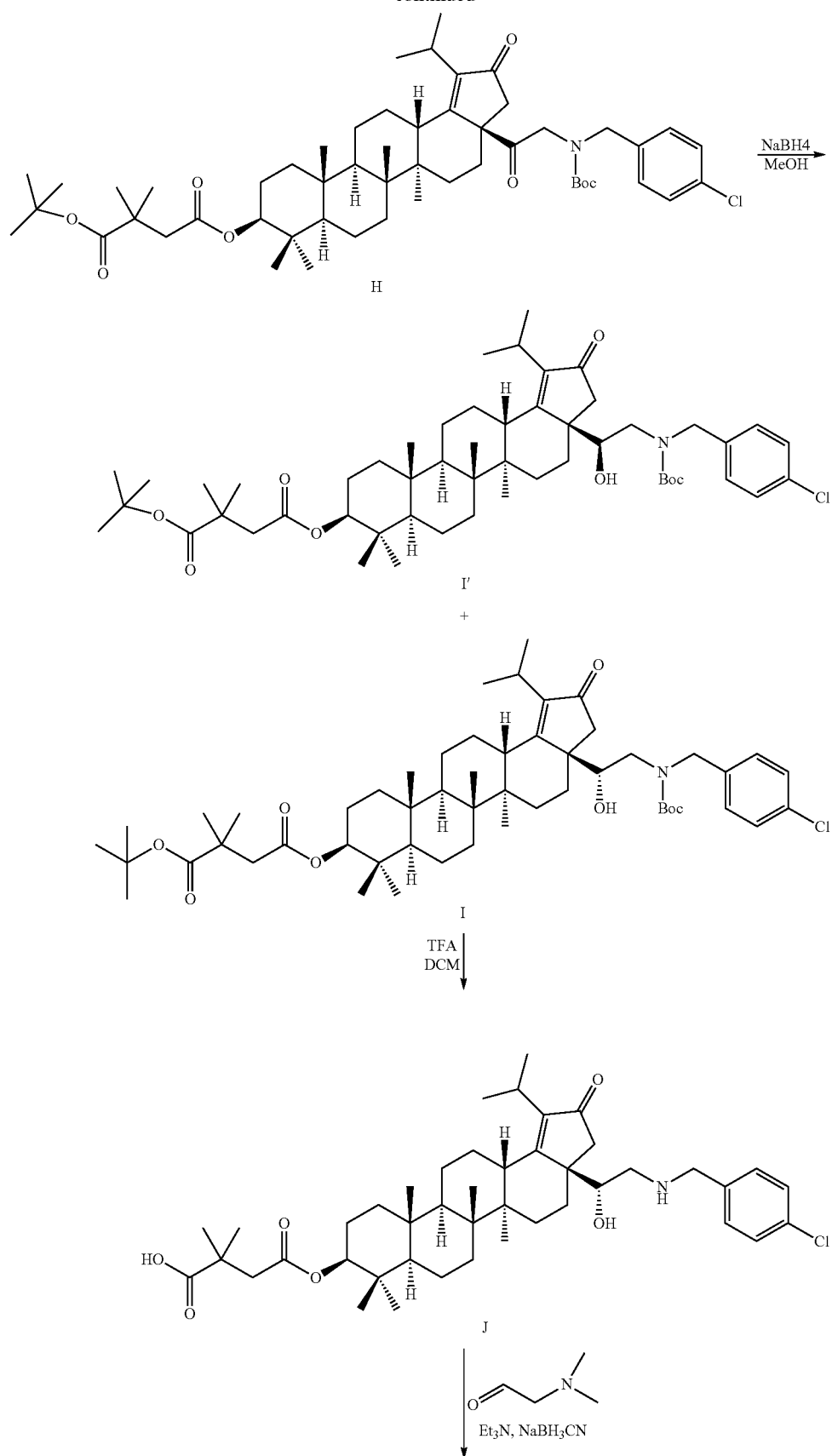


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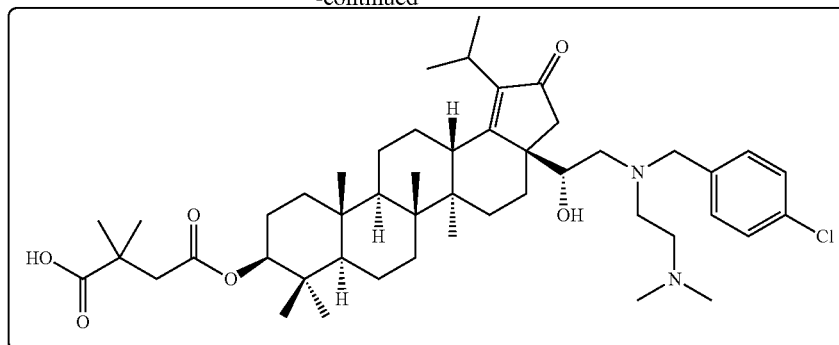
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Administration and Formulation

In another embodiment, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable diluent and a therapeutically effective amount of a compound of Formula I or Formula II or a pharmaceutically acceptable salt thereof.

The compounds of the present invention can be supplied in the form of a pharmaceutically acceptable salt. The terms "pharmaceutically acceptable salt" refer to salts prepared from pharmaceutically acceptable inorganic and organic acids and bases. Accordingly, the word "or" in the context of "a compound or a pharmaceutically acceptable salt thereof" is understood to refer to either a compound or a pharmaceutically acceptable salt thereof (alternative), or a compound and a pharmaceutically acceptable salt thereof (in combination).

As used herein, the term "pharmaceutically acceptable" refers to those compounds, materials, compositions, and dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, or other problem or complication. The skilled artisan will appreciate that pharmaceutically acceptable salts of compounds according to Formula I or Formula II may be prepared. These pharmaceutically acceptable salts may be prepared in situ during the final isolation and purification of the compound, or by separately reacting the purified compound in its free acid or free base form with a suitable base or acid, respectively.

Illustrative pharmaceutically acceptable acid salts of the compounds of the present invention can be prepared from the following acids, including, without limitation formic, acetic, propionic, benzoic, succinic, glycolic, gluconic, lactic, maleic, malic, tartaric, citric, nitic, ascorbic, glucuronic, maleic, fumaric, pyruvic, aspartic, glutamic, benzoic, hydrochloric, hydrobromic, hydroiodic, isocitric, trifluoroacetic, pamoic, propionic, anthranilic, mesylic, oxalacetic, oleic, stearic, salicylic, p-hydroxybenzoic, nicotinic, phenylacetic, mandelic, embonic (pamoic), methanesulfonic, phosphoric, phosphonic, ethanesulfonic, benzenesulfonic, pantothenic, toluenesulfonic, 2-hydroxyethanesulfonic, sulfanilic, sulfuric, salicylic, cyclohexylaminosulfonic, algenic, β -hydroxybutyric, galactaric and galacturonic acids. Preferred pharmaceutically acceptable salts include the salts of hydrochloric acid and trifluoroacetic acid.

Illustrative pharmaceutically acceptable inorganic base salts of the compounds of the present invention include metallic ions. More preferred metallic ions include, but are not limited to, appropriate alkali metal salts, alkaline earth metal salts and other physiological acceptable metal ions. Salts derived from inorganic bases include aluminum, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganese salts, manganous, potassium, sodium, zinc, and the like

and in their usual valences. Exemplary base salts include aluminum, calcium, lithium, magnesium, potassium, sodium and zinc. Other exemplary base salts include the ammonium, calcium, magnesium, potassium, and sodium salts. Still other exemplary base salts include, for example, hydroxides, carbonates, hydrides, and alkoxides including NaOH, KOH, Na_2CO_3 , K_2CO_3 , NaH, and potassium-t-butoxide.

Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, including in part, trimethylamine, diethylamine, N,N'-dibenzylethylenediamine, chlorprocaine, choline, diethanolamine, ethylenediamine, meglumine (N-methylglucamine) and procaine; substituted amines including naturally occurring substituted amines; cyclic amines; quaternary ammonium cations; and basic ion exchange resins, such as arginine, betaine, caffeine, choline, N,N-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine and the like.

All of the above salts can be prepared by those skilled in the art by conventional means from the corresponding compound of the present invention. For example, the pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. The salt may precipitate from solution and be collected by filtration or may be recovered by evaporation of the solvent. The degree of ionisation in the salt may vary from completely ionised to almost non-ionised. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, Pa., 1985, p. 1418, the disclosure of which is hereby incorporated by reference only with regards to the lists of suitable salts.

The compounds of the invention may exist in both unsolvated and solvated forms. The term 'solvate' is used herein to describe a molecular complex comprising the compound of the invention and one or more pharmaceutically acceptable solvent molecules, for example, ethanol. The term 'hydrate' is employed when said solvent is water. Pharmaceutically acceptable solvates include hydrates and other solvates wherein the solvent of crystallization may be isotopically substituted, e.g. D_2O , d_6 -acetone, d_6 -DMSO.

Compounds of Formula I or Formula II containing one or more asymmetric carbon atoms can exist as two or more stereoisomers. Where a compound of Formula I or Formula II

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contains an alkenyl or alkenylene group or a cycloalkyl group, geometric cis/trans (or Z/E) isomers are possible. Where the compound contains, for example, a keto or oxime group or an aromatic moiety, tautomeric isomerism ('tautomerism') can occur. It follows that a single compound may exhibit more than one type of isomerism.

Included within the scope of the claimed compounds present invention are all stereoisomers, geometric isomers and tautomeric forms of the compounds of Formula I or Formula II, including compounds exhibiting more than one type of isomerism, and mixtures of one or more thereof. Also included are acid addition or base salts wherein the counterion is optically active, for example, D-lactate or L-lysine, or racemic, for example, DL-tartrate or DL-arginine.

Cis/trans isomers may be separated by conventional techniques well known to those skilled in the art, for example, chromatography and fractional crystallisation.

Conventional techniques for the preparation/isolation of individual enantiomers include chiral synthesis from a suitable optically pure precursor or resolution of the racemate (or the racemate of a salt or derivative) using, for example, chiral high pressure liquid chromatography (HPLC).

Alternatively, the racemate (or a racemic precursor) may be reacted with a suitable optically active compound, for example, an alcohol, or, in the case where the compound of Formula I or Formula II contains an acidic or basic moiety, an acid or base such as tartaric acid or 1-phenylethylamine. The resulting diastereomeric mixture may be separated by chromatography and/or fractional crystallization and one or both of the diastereoisomers converted to the corresponding pure enantiomer(s) by means well known to a skilled person.

Chiral compounds of the invention (and chiral precursors thereof) may be obtained in enantiomerically-enriched form using chromatography, typically HPLC, on a resin with an asymmetric stationary phase and with a mobile phase consisting of a hydrocarbon, typically heptane or hexane, containing from 0 to 50% isopropanol, typically from 2 to 20%, and from 0 to 5% of an alkylamine, typically 0.1% diethylamine. Concentration of the eluate affords the enriched mixture.

Mixtures of stereoisomers may be separated by conventional techniques known to those skilled in the art. [see, for example, "Stereochemistry of Organic Compounds" by E L Eliel (Wiley, New York, 1994).]

The present invention includes all pharmaceutically acceptable isotopically-labelled compounds of Formula I or Formula II wherein one or more atoms are replaced by atoms having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number usually found in nature.

Examples of isotopes suitable for inclusion in the compounds of the invention include isotopes of hydrogen, such as ^2H and ^3H , carbon, such as ^{11}C , ^{13}C and ^{14}C , chlorine, such as ^{36}Cl , fluorine, such as ^{18}F , iodine, such as ^{123}I and ^{125}I , nitrogen, such as ^{13}N and ^{15}N , oxygen, such as ^{15}O , ^{17}O and ^{18}O , phosphorus, such as ^{32}P , and sulphur, such as ^{35}S .

Certain isotopically-labelled compounds of Formula I or Formula II, for example, those incorporating a radioactive isotope, are useful in drug and/or substrate tissue distribution studies. The radioactive isotopes tritium, i.e. ^3H , and carbon-14, i.e. ^{14}C , are particularly useful for this purpose in view of their ease of incorporation and ready means of detection.

Substitution with heavier isotopes such as deuterium, i.e. ^2H , may afford certain therapeutic advantages resulting from greater metabolic stability, for example, increased in vivo half-life or reduced dosage requirements, and hence may be preferred in some circumstances.

Isotopically-labelled compounds of Formula I or Formula II can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying Examples and Prepara-

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tions using an appropriate isotopically-labelled reagents in place of the non-labelled reagent previously employed.

The compounds of the present invention may be administered as prodrugs. Thus, certain derivatives of compounds of Formula I or Formula II, which may have little or no pharmacological activity themselves can, when administered into or onto the body, be converted into compounds of Formula I or Formula II as 'prodrugs'.

Administration of the chemical entities described herein can be via any of the accepted modes of administration for agents that serve similar utilities including, but not limited to, orally, sublingually, subcutaneously, intravenously, intranasally, topically, transdermally, intraperitoneally, intramuscularly, intrapulmonarily, vaginally, rectally, or intraocularly. In some embodiments, oral or parenteral administration is used.

Pharmaceutical compositions or formulations include solid, semi-solid, liquid and aerosol dosage forms, such as, e.g., tablets, capsules, powders, liquids, suspensions, suppositories, aerosols or the like. The chemical entities can also be administered in sustained or controlled release dosage forms, including depot injections, osmotic pumps, pills, transdermal (including electrotransport) patches, and the like, for prolonged and/or timed, pulsed administration at a predetermined rate. In certain embodiments, the compositions are provided in unit dosage forms suitable for single administration of a precise dose.

The chemical entities described herein can be administered either alone or more typically in combination with a conventional pharmaceutical carrier, excipient or the like (e.g., mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, sodium crosscarmellose, glucose, gelatin, sucrose, magnesium carbonate, and the like). If desired, the pharmaceutical composition can also contain minor amounts of nontoxic auxiliary substances such as wetting agents, emulsifying agents, solubilizing agents, pH buffering agents and the like (e.g., sodium acetate, sodium citrate, cyclodextrine derivatives, sorbitan monolaurate, triethanolamine acetate, triethanolamine oleate, and the like). Generally, depending on the intended mode of administration, the pharmaceutical composition will contain about 0.005% to 95%; in certain embodiments, about 0.5% to 50% by weight of a chemical entity. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see *Remington's Pharmaceutical Sciences*, Mack Publishing Company, Easton, Pa.

In certain embodiments, the compositions will take the form of a pill or tablet and thus the composition will contain, along with the active ingredient, a diluent such as lactose, sucrose, dicalcium phosphate, or the like; a lubricant such as magnesium stearate or the like; and a binder such as starch, gum acacia, polyvinylpyrrolidone, gelatin, cellulose, cellulose derivatives or the like. In another solid dosage form, a powder, marume, solution or suspension (e.g., in propylene carbonate, vegetable oils or triglycerides) is encapsulated in a gelatin capsule.

Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, etc. at least one chemical entity and optional pharmaceutical adjuvants in a carrier (e.g., water, saline, aqueous dextrose, glycerol, glycols, ethanol or the like) to form a solution or suspension. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions, as emulsions, or in solid forms suitable for dissolution or suspension in liquid prior to injection. The percentage of chemical entities contained in such parenteral compositions is highly dependent on the specific nature thereof, as well as the activity of the chemical entities and the needs of the subject. However, percentages of active ingredient of 0.01% to 10% in solution are employable, and will be higher if the composition is a solid which will be subsequently diluted to the above percentages.

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In certain embodiments, the composition will comprise from about 0.2 to 2% of the active agent in solution.

Pharmaceutical compositions of the chemical entities described herein may also be administered to the respiratory tract as an aerosol or solution for a nebulizer, or as a microfine powder for insufflation, alone or in combination with an inert carrier such as lactose. In such a case, the particles of the pharmaceutical composition have diameters of less than 50 microns, in certain embodiments, less than 10 microns.

In general, the chemical entities provided will be administered in a therapeutically effective amount by any of the accepted modes of administration for agents that serve similar utilities. The actual amount of the chemical entity, i.e., the active ingredient, will depend upon numerous factors such as the severity of the disease to be treated, the age and relative health of the subject, the potency of the chemical entity used the route and form of administration, and other factors. The drug can be administered more than once a day, such as once or twice a day.

Therapeutically effective amounts of the chemical entities described herein may range from approximately 0.01 to 200 mg per kilogram body weight of the recipient per day; such as about 0.01-100 mg/kg/day, for example, from about 0.1 to 50 mg/kg/day. Thus, for administration to a 70 kg person, the dosage range may be about 7-3500 mg per day.

In general, the chemical entities will be administered as pharmaceutical compositions by any one of the following routes: oral, systemic (e.g., transdermal, intranasal or by suppository), or parenteral (e.g., intramuscular, intravenous or subcutaneous) administration. In certain embodiments, oral administration with a convenient daily dosage regimen that can be adjusted according to the degree of affliction may be used. Compositions can take the form of tablets, pills, capsules, semisolids, powders, sustained release formulations, solutions, suspensions, elixirs, aerosols, or any other appropriate compositions. Another manner for administering the provided chemical entities is inhalation.

The choice of formulation depends on various factors such as the mode of drug administration and bioavailability of the drug substance. For delivery via inhalation the chemical entity can be formulated as liquid solution, suspensions, aerosol propellants or dry powder and loaded into a suitable dispenser for administration. There are several types of pharmaceutical inhalation devices-nebulizer inhalers, metered dose inhalers (MDI) and dry powder inhalers (DPI). Nebulizer devices produce a stream of high velocity air that causes the therapeutic agents (which are formulated in a liquid form) to spray as a mist that is carried into the patient's respiratory tract. MDIs typically are formulation packaged with a compressed gas. Upon actuation, the device discharges a measured amount of therapeutic agent by compressed gas, thus affording a reliable method of administering a set amount of agent. DPI dispenses therapeutic agents in the form of a free flowing powder that can be dispersed in the patient's inspiratory air-stream during breathing by the device. In order to achieve a free flowing powder, the therapeutic agent is formulated with an excipient such as lactose. A measured amount of the therapeutic agent is stored in a capsule form and is dispensed with each actuation.

Recently, pharmaceutical compositions have been developed for drugs that show poor bioavailability based upon the principle that bioavailability can be increased by increasing the surface area i.e., decreasing particle size. For example, U.S. Pat. No. 4,107,288 describes a pharmaceutical formulation having particles in the size range from 10 to 1,000 nm in which the active material is supported on a cross-linked matrix of macromolecules. U.S. Pat. No. 5,145,684 describes the production of a pharmaceutical formulation in which the drug substance is pulverized to nanoparticles (average particle size of 400 nm) in the presence of a surface modifier and then dispersed in a liquid medium to give a pharmaceutical formulation that exhibits remarkably high bioavailability.

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The compositions are comprised of, in general, at least one chemical entity described herein in combination with at least one pharmaceutically acceptable excipient. Acceptable excipients are non-toxic, aid administration, and do not adversely affect the therapeutic benefit of the at least one chemical entity described herein. Such excipient may be any solid, liquid, semi-solid or, in the case of an aerosol composition, gaseous excipient that is generally available to one of skill in the art.

Solid pharmaceutical excipients include starch, cellulose, talc, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, magnesium stearate, sodium stearate, glycerol monostearate, sodium chloride, dried skim milk and the like. Liquid and semisolid excipients may be selected from glycerol, propylene glycol, water, ethanol and various oils, including those of petroleum, animal, vegetable or synthetic origin, e.g., peanut oil, soybean oil, mineral oil, sesame oil, etc. Liquid carriers, for injectable solutions, include water, saline, aqueous dextrose, and glycols.

Compressed gases may be used to disperse a chemical entity described herein in aerosol form. Inert gases suitable for this purpose are nitrogen, carbon dioxide, etc. Other suitable pharmaceutical excipients and their formulations are described in Remington's Pharmaceutical Sciences, edited by E. W. Martin (Mack Publishing Company, 18th ed., 1990).

The amount of the chemical entity in a composition can vary within the full range employed by those skilled in the art. Typically, the composition will contain, on a weight percent (wt %) basis, from about 0.01-99.99 wt % of at least one chemical entity described herein based on the total composition, with the balance being one or more suitable pharmaceutical excipients. In certain embodiments, the at least one chemical entity described herein is present at a level of about 1-80 wt %.

Example 84

MT4 Cell Antiviral Assay

Experimental Procedure

Antiviral HIV activity and compound-induced cytotoxicity were measured in parallel by means of a propidium iodide based procedure in the human T-cell lymphotropic virus transformed cell line MT4. Aliquots of the test compounds were serially diluted in medium (RPMI 1640, 10% fetal calf serum (FCS), and gentamycin) in 96-well plates (Costar 3598) using a Cetus Pro/Pette. Exponentially growing MT4 cells were harvested and centrifuged at 1000 rpm for 10 min in a Jouan centrifuge (model CR 4 12). Cell pellets were resuspended in fresh medium (RPMI 1640, 20% FCS, 20% IL-2, and gentamycin) to a density of 5×10^5 cells/ml. Cell aliquots were infected by the addition of HIV-1 (strain 111B) diluted to give a viral multiplicity of infection of $100 \times$ TCID₅₀. A similar cell aliquot was diluted with medium to provide a mock-infected control. Cell infection was allowed to proceed for 1 hr at 37° C. in a tissue culture incubator with humidified 5% CO₂ atmosphere. After the 1 hr incubation the virus/cell suspensions were diluted 6-fold with fresh medium, and 125 μ l of the cell suspension was added to each well of the plate containing pre-diluted compound. Plates were then placed in a tissue culture incubator with humidified 5% CO₂ for days. At the end of the incubation period, cell number and hence HIV-induced cytopathology was estimated by either (A) propidium iodide staining, or by an (B) MTS tetrazolium staining method.

For propidium iodide readout, 27 μ l of 5% Nonidet-40 was added to each well of the incubation plate. After thorough mixing with a Costar multitip pipetter, 60 μ l of the mixture was transferred to filter-bottomed 96-well plates. The plates were analyzed in an automated assay instrument (Screen

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Machine, Idexx Laboratories). The control and standard used was 3'-azido-3'-deoxythymidine tested over a concentration range of 0.01 to 1 μ M in every assay. The expected range of IC_{50} values for 3'-azido-3'-deoxythymidine is 0.04 to 0.12 μ M. The assay makes use of a propidium iodide dye to estimate the DNA content of each well.

For MTS readout, 20 μ l CellTiter 96 AQ One Solution reagent (Promega #G3582) was added to each well. At 75 minutes following the addition of MTS reagent, absorbance was read at 492 nm using a Tecan Sunrise 96-well plate reader.

Analysis:

The antiviral effect of a test compound is reported as an EC_{50} , i.e. the inhibitory concentration that would produce a 50% decrease in the HIV-induced cytopathic effect. This effect is measured by the amount of test compound required to restore 50% of the cell growth of HIV-infected MT4 cells, compared to uninfected MT4 cell controls. IC_{50} was calculated by RoboSage, Automated Curve Fitting Program, version 5.00, 10 Jul. 1995.

For each assay plate, the results (relative fluorescence units, rFU, or OD values) of wells containing uninfected cells or infected cells with no compound were averaged, respectively. For measurements of compound-induced cytotoxicity, results from wells containing various compound concentrations and uninfected cells were compared to the average of uninfected cells without compound treatment. Percent of cells remaining is determined by the following formula:

$$\text{Percent of cells remaining} = (\text{compound-treated uninfected cells, rFU, or OD values} / \text{untreated uninfected cells}) \times 100.$$

A level of percent of cells remaining of 79% or less indicates a significant level of direct compound-induced cytotoxicity for the compound at that concentration. When this condition occurs the results from the compound-treated infected wells at this concentration are not included in the calculation of EC_{50} .

For measurements of compound antiviral activity, results from wells containing various compound concentrations and infected cells are compared to the average of uninfected and infected cells without compound treatment. Percent inhibition of virus is determined by the following formula:

$$\text{Percent inhibition of virus} = (1 - ((\text{ave. untreated uninfected cells} - \text{treated infected cells}) / (\text{ave. untreated uninfected cells} - \text{ave. untreated infected cells}))) \times 100.$$

Results:

Compounds of the present invention have anti-HIV activity in the range EC_{50} =1-1000 nM.

Table 3 shows EC_{50} values for representative compounds of Table 2 after the HIV MT4 Antiviral Cell Assay of Example 84.

TABLE 3

Example number	EC_{50} NL4-3 wt (nM)	EC_{50} V370A (nM)
1	41.1	34.6
2	5.2	4.7
3	61.7	242.7
4	10.1	9.3
5	2.6	3.2
6	0.5	3.8
7	6.1	23.1
8	5.9	14.3
9	12.3	13.5
10	2.3	2.4
11	6.3	6.7
12	4.5	5.1
13	1.6	2.1
14	2.1	3.6
15	6.9	31.1

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TABLE 3-continued

Example number	EC_{50} NL4-3 wt (nM)	EC_{50} V370A (nM)
16	11.0	7.6
17	8.7	29.2
18	0.8	0.7
19	3.9	4.1
20	2.3	4.1
21	76.5	103.5
22	3.3	3.5
23	4.9	11.7
24	40.4	1528.0
25	14.7	27.8
26	4.9	545.0
27	8.2	8.9
29	17.5	28.6
31	5.4	22.5
33	5.3	ND
34	7.1	21.1
35	4.2	124.0
36	4.0	9.4
37	26.9	556.6
38	5.2	20.9
39	6.6	217.1
40	11.1	18.9
44	1.8	2.6
45	1.9	2.5
46	11.1	64.8
47	7.7	72.9
49	21.8	192.3
50	1.1	1.4
51	3.5	6.3
52	4.6	7.0
53	6.2	494.3
56	3.4	3.4
57	4.2	8.0
58	31.5	379.0
59	5.3	17.2
60	60.2	8409.0
61	129.7	10000.0
62	103.6	213.2
63	3.2	5.0
64	7.2	120.2
65	83.8	3077.0
66	9.2	16.1
67	135.5	411.1
68	10.5	110.2
69	1.0	4.1
70	1.6	2.1
71	31.2	35.3
72	5.1	10.8
73	31.8	62.3
74	2.9	4.8
75	0.6	1.0
76	0.7	0.9
77	4.7	5.0
78	2.1	2.7
79	14.7	76.1
80	2.4	2.7
81	3.0	5.4
82	8.9	70.5
83	7.3	143.5

Example 86

This example shows the EC_{50} potencies of Bevirimat, compound 51, compound A, and compound B against wild type HIV, site directed HIV mutants, and clinical HIV isolates. As can be seen in Table 5, compound 51 demonstrates higher potency than the other compounds when measured against HIV among wildtype, certain site directed mutants, and against several clinical HIV isolates. Surprisingly, compound 51 continues to have excellent potency against HIV relative to the other compounds, when protein binding is taken into account as can be seen in Table 6.

The results in Tables 5 and 6 for compound 51 demonstrate an unexpected result taken in light of Bevirimat and compounds A and B. The results in the above tables are indicative

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of the unpredictability in developing anti-HIV compounds where a subtle change in the chemical structure can have a large impact on the clinical result. Where compounds A and B show alternating efficacy in their both their EC₅₀ values for polymorphism and protein binding, compound 51 shows none of this variability and is therefore unexpectedly superior when viewed in terms of potential clinical applicability. A direct comparison between compound 51 and compounds A and B, demonstrate how subtle chemical substitutions can have a dramatic effect on the in vitro efficacy of a putative anti-HIV compound.

A similar advantage for compound 51 can be seen in Table 6 where protein binding and serum shift for the above compounds are compared. This table shows both a significant decrease in the EC₅₀ and a reduced serum effect for compound 51 relative to the other compounds tested.

TABLE 5

Wild-type, Polymorphisms, & PBLs - EC ₅₀ (nM)					
	MT4 NL. wt*	MT4 NL. V370A	HIV-1 B CC1/85 (V370A)	HIV-1 B ASJM108 (V370A+)	HIV-1 C 972A009 (V370A+)
Bevirimat	223	6062	>10000	>10000	13435
Compound A	14	16	5	51	1159
Compound B	8	8	13	6	2000
Compound 51	0.8	0.7	1.2	1.0	4

*Consensus Clade B Sp1 Genotype.

TABLE 6

Protein Binding Effects on Potency			
	LHIV IC ₅₀ (nM)	LHIV IC ₅₀ (nM) with 40% HuS	Fold shift with 40% HuS
Bevirimat	42	6600	157
Compound A	9.3	73	7.9
Compound B	3.2	43	13.4
Compound 51	1.9	10.6	5.5 ^a

^aDefinitive protein shift value determined in PBL's by titration at SRI is 1X

Example 87

It is suspected that many anti-HIV compounds might potentially be less effective in the treatment of patients who have failed a previous protease inhibitor-containing regimen and whose viruses have developed drug resistance mutations within the protease gene.

A major obstacle to their long-term efficacy of anti-HIV therapies has been the emergence of resistance to current antiretroviral drugs. One method for comparing the effectiveness of anti-HIV compounds is the characterization of such compounds' polymorphism at drug resistant sites.

A comparison of compound 51 versus Bevirimat ("BVM") against a broad panel of HIV isolates is shown in FIG. 1. From FIG. 1, it can be seen that compound 51 shows superior polymorphism coverage across this panel of HIV isolates to Bevirimat. Likewise, compound 51 shows superior polymorphism coverage as compared to compound C as shown in FIG. 2.

This example was performed as follows. Crude human primary blood mononuclear cells (PBMCs) were collected from healthy donors via leukapheresis and determined to be negative for HIV exposure, among a variety of additional infectious diseases. PBMCs were isolated via Ficoll-Hypaque density gradient separation followed by aspiration of the banded leukocytes from the gradient. Purified PBMCs

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from 10 individual donors were combined and cryopreserved in liquid nitrogen as a PBMC pool. Various PBMC pools were utilized.

Various HIV-1 isolates were obtained from different sources. A stock of the virus was generated in a pool of CD4+ PBMCs and frozen. Viral replication for each virus stock was measured on PHA-blasted PBMC pools to determine the appropriate virus input for anti-viral assays. HIV gag sequences were determined for each isolate by the Sanger di-deoxy sequencing method.

Cryo-preserved PBMC pools were thawed and stimulated with 2 µg/mL PHA in media (RPMI1640, 20% FBS, 10% T cell growth factor, antibiotics) for 3 days. Blasts were then washed, counted, and cultured in media at 2×10⁶ cells/mL in media with 10 U/mL recombinant IL-2 for an additional 24 hours. Stimulated PBMCs were counted for trypan blue exclusion viability and seeded in 96-well round bottom plates at a final density of 1×10⁶ cells/well. A volume of the drug dose titration was added to the cells followed by a predetermined amount of virus. The plates were incubated for 7 days at 37° C., 5% CO₂, to allow for viral replication and inhibition by compound to assess anti-viral potency.

In order to determine anti-viral potency, HIV reverse transcriptase activity in cell culture supernatants was measured as a measure of viral replication in the presence or absence of compound. At the end of the incubation period, fifty (50) µL of PBMC culture supernatants were transferred to a new 96-well plate; 10 µL of RT extraction buffer was added followed by the addition of 40 µL of RT assay buffer. The RT plates were thoroughly mixed and placed in a humidified incubator at 37° C., 5% CO₂ for 2 h. DE-81 96-well plates were placed on a vacuum manifold and 100 µL of the RT reaction transferred to the ion-exchange chromatography plates. After applying the solution phase of the RT reaction to the DE-81 plate, the plate was then washed once with prepared 5% Na₂HPO₄, followed by a wash of dH₂O. Plates were then allowed to dry overnight at room temperature. The plates were sealed and 50 µL scintillation fluid added prior to reading on a Topcount (Packard) luminometer at 10 s/well.

Below are the particular HIV-1 isolates tested as shown in FIG. 1:

- 1—HIV-1 A_UG275
- 2—HIV-1 AE_42368
- 3—HIV-1 C_97/ZA/009
- 4—HIV-1 C_ETH2220
- 5—HIV-1 C_ZAM18
- 6—HIV-1 C_I-2516
- 7—HIV-1 B_CC1/85
- 8—HIV-1 B_ASJM108
- 9—HIV-1 B_SF162
- 10—HIV-1 B_92US657
- 11—HIV-1 B_BR92030
- 12—HIV-1 B_ASM42
- 13—HIV-1 B_BR92023
- 14—HIV-1 B_ASM44
- 15—HIV-1 B_92US660
- 16—HIV-1 B_THA92014
- 17—HIV-1 B_IIIB
- 18—HIV-1 B_301596
- 19—HIV-1 B_ASM34
- 20—HIV-1 B_BK132
- 21—HIV-1 B_ASM57
- 22—HIV-1 B_ASM54
- 23—HIV-1 B_92HT599
- 24—HIV-1 B_CM237
- 25—HIV-1 B_92HT593
- 26—HIV-1 B_BZ167
- 27—HIV-1 B_92US723

Below are the particular HIV isolates tested as shown in FIG. 2:

- 1—HIV-1 A_UG275
- 2—HIV-1 AE_42368

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3—HIV-1 B_301596
 4—HIV-1 B_92HT593
 5—HIV-1 B_92HT599
 6—HIV-1 B_92US657
 7—HIV-1 B_92US660
 8—HIV-1 B_92US723
 9—HIV-1 B_ASJM108
 10—HIV-1 B_ASM34
 11—HIV-1 B_ASM42
 12—HIV-1 B_ASM44
 13—HIV-1 B_ASM54
 14—HIV-1 B_BK132
 15—HIV-1 B_BZ167
 16—HIV-1 B_CC1/85
 17—HIV-1 B_CM237
 18—HIV-1 B_IIIB
 19—HIV-1 B_SF162
 20—HIV-1 C_97/ZA/009
 21—HIV-1 C_ETH2220
 22—HIV-1 C_ZAM18

Example 88

This example shows in Table 7a direct comparison between compound 51, compound 56, and compound C. Intrinsic HIV wild type potency for compound 51 relative to compound C is about 100× better (0.8 nM vs. 6 nM). In the HIV polymorphic strain, V370, the potency for compound 51 relative to compound C is even more dramatic (0.7 nM vs. 19 nM). In terms of human protein shift listed as human serum (HS) in this example, is another factor of 10 fold better for compound 51 relative to compound C (5.5 fold shift vs. a 48.9 fold shift).

All taken together, as can be seen in Table 7 there is a factor of 238 fold improvement for compound 51 over compound C for the C_{trough} target, which is the $PAEC_{50}$ (or $PAEC_{90}$ which is the same factor just higher for each by a factor of 3-4 fold). In fact, the reported 5.5 fold shift in Table 7 for 40% human serum in a multicell HIV full life cycle reporter based assay.

Table 7 also depicts the protein adjusted EC_{50} for the V370A polymorphic virus (which represents up to 40% of patients in clade B and maybe more outside clade B) you can see that compound 51 potency is unexpectedly greater at 3.9 nM, while compound C potency is lower at 929 nM.

TABLE 7

Compound Identity	HIV w/t $MT^A EC_{50}$	V370A $MT^A EC_{50}$	Human Serum Fold Shift**	V370A $PAEC_{50}$ ***
Compound 51 ('232)	0.8 nM	0.7 nM	5.5X	3.9 nM
Compound 56 ('233)	4 nM	4 nM	16.2X	65 nM
Compound C ('363)	6 nM	19 nM	48.9X	929 nM

**Human Serum fold shift values determined using 40% human serum in a HIV multicell full life cycle assay.

***V370A $PAEC_{50}$ is determined by the product of V370A $MT^A EC_{50}$ and human serum fold shift.

Example 89

The PBL assay in this example was performed as follows in order to study the effect of human serum on the HIV antiviral activity of certain compounds. In particular, the effect of the presence of human serum on the antiviral activity of compound 51 and Bevirimat ("BVM") was evaluated in a modified PMBC assay.

In the standard assay, PHA/IL-2 stimulated PBMCs (5×10^4 cells/well) were incubated with virus and compound 51 or BVM (both compounds tested at range of 0.06 nM to 25 mM) for 7 days.

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In the modified PBMC assay, PHA/IL-2 stimulated PBMCs were pre-incubated with HIV-1 strain JR-CSF prior to addition of compound 51 or BVM and human serum. In this assay, 8×10^5 cells from pooled donors were incubated with virus for 1 hour, followed by centrifugation for 1 hour. Cells were then gently re-suspended and incubated an additional 2 hours. During this second incubation period, 2.5×10^4 uninfected PBMCs from pooled donors were added to the interior 60 wells of a 96 well plate, followed by the addition of compound 51 or BVM (both compounds tested at range of 0.06 nM to 25 mM) and human serum (10%, 20%, 30% and 40%) to the appropriate wells. At the end of the second incubation period, infected cells were diluted in media (5×10^5 cells/mL) (without washout of virus) and 50 mL (2.5×10^4 cells) were added to each well of the plate and incubated for 7 days.

Following incubation in both the standard and modified assays, supernatants were assayed for reverse transcriptase (RT) activity and p24 antigen content by ELISA and spectrophotometric analysis at 450 nM.

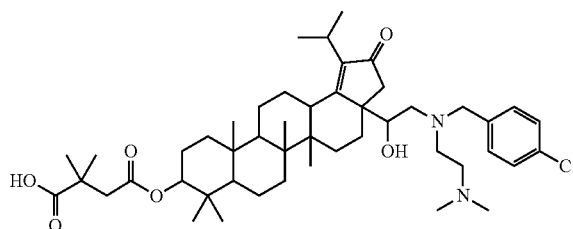
Compound 51 maintained antiviral activity in the presence of human serum at all serum concentrations tested, with no apparent shift in IC_{50} values (range: 0.52 to 3.07 nM) compared to the IC_{50} value (0.69 nM) in the standard assay (0% serum). These results indicate that the inhibitory activity of compound 51 is minimally or not at all impacted by serum proteins. Extrapolating from the normalized IC_{50} values observed in the presence of the various human serum concentrations gave an estimated IC_{50} value of 0.33 nM for 100% human serum (assuming a linear relationship). BVM also maintained antiviral activity in the presence of human serum at all concentrations, however, there was a large increase in the IC_{50} values (range: 1.38 mM to 13 mM) associated with increasing human serum concentrations compared to the standard assay (9.76 nM). Extrapolating from the normalized IC_{50} values observed in the presence of the various concentrations of human serum there is a 2.310-fold change in the IC_{50} value in the presence of 100% serum (compared to the control experiment, suggesting that BVM is highly bound by serum proteins).

The effect of human serum on antiviral activity of compound 51 and BVM was also evaluated in the LHIV assay. Using the same format as the standard LHIV assay, the addition of 40% human serum caused a 5.6-fold shift in the IC_{50} value (10.6 nM) for compound 51 and a 174.9-fold shift in IC_{50} value (3.88 mM) for BVM.

However, when determined in a PBL assay containing a titration between 0 and 40% human serum the extrapolated value is 1 fold or less. Therefore, the improvement of compound 51 over compound C, in terms of potency while in the presence of human serum, is likely >1300 fold better when a more typical baseline is taken into account. See FIGS. 3, 4, and 5.

What is claimed is:

1. A compound of the structure:

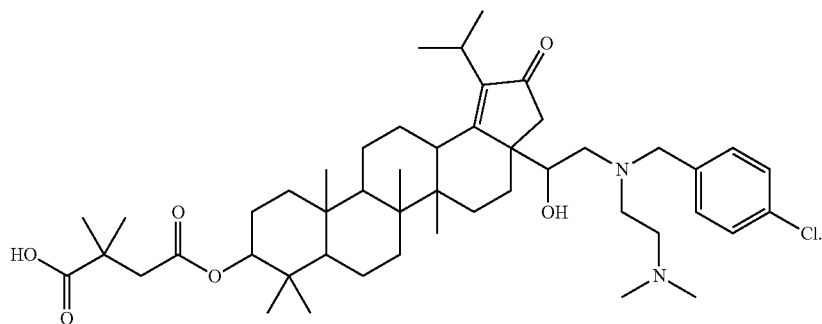


or a pharmaceutical acceptable salt thereof.

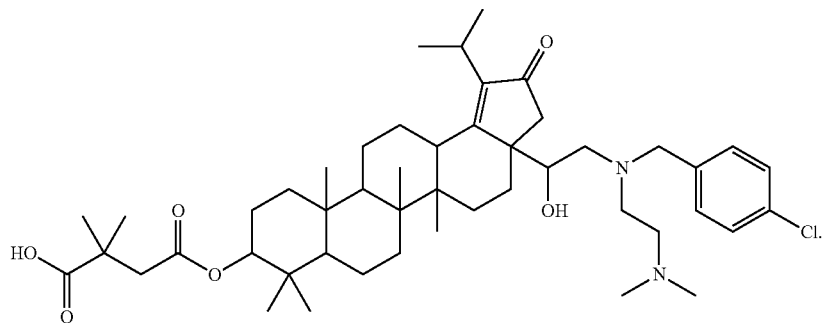
661

662

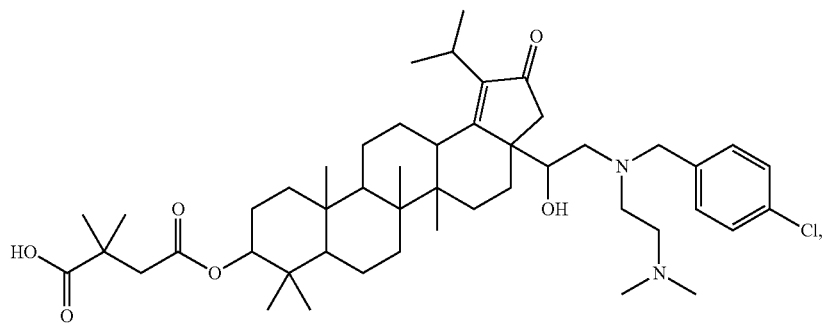
2. compound of the structure:



3. A pharmaceutically acceptable salt of a compound of the structure: ²⁰

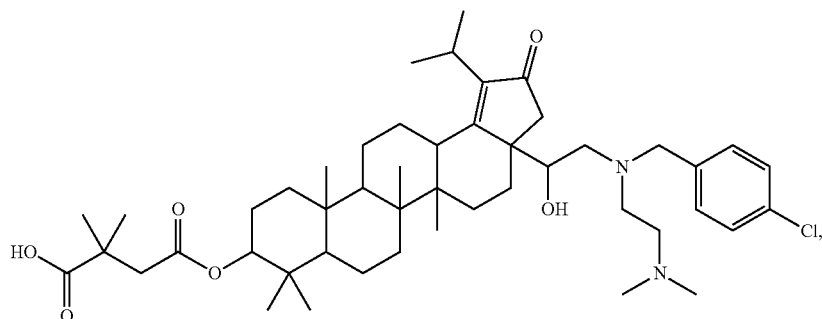


4. A pharmaceutical composition comprising a compound of the structure:



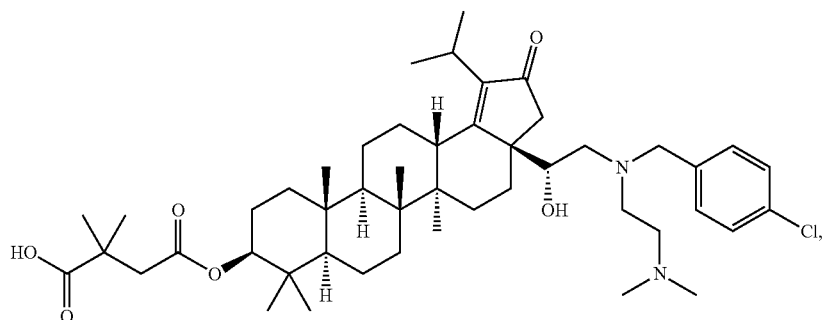
together with at least one pharmaceutically acceptable excipient. ⁶⁵

5. A pharmaceutical composition comprising a compound of the structure:



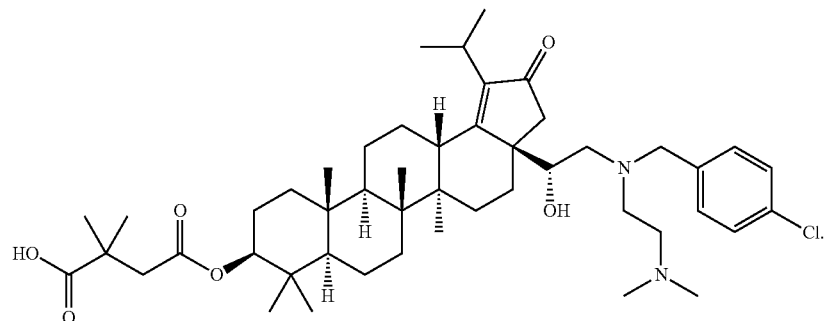
or a pharmaceutically acceptable salt thereof, together with at least one pharmaceutically acceptable excipient.

6. A compound of the structure:



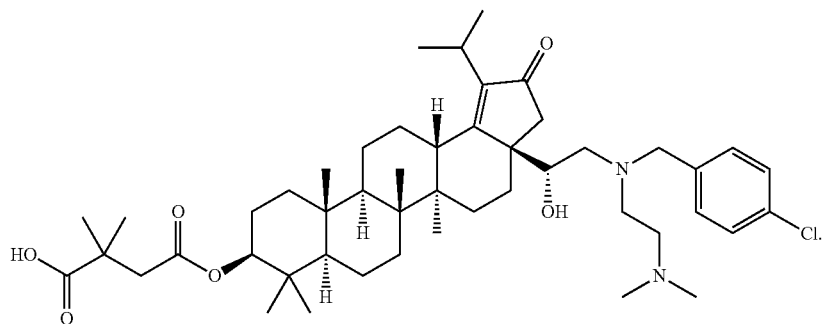
or a pharmaceutically acceptable salt thereof.

7. A compound of the structure:



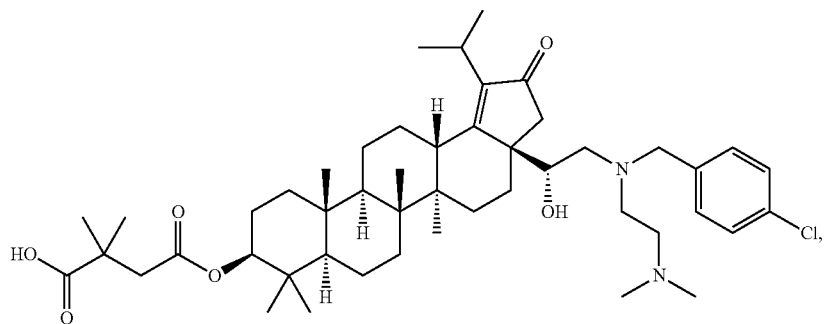
665

8. A pharmaceutically acceptable salt of a compound of the structure:



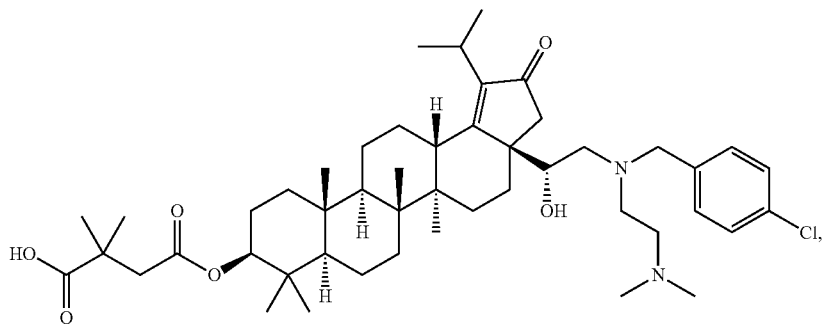
666

9. A pharmaceutical composition comprising a compound of the structure:



together with at least one pharmaceutically acceptable excipient.

10. A pharmaceutical composition comprising a compound of the structure:



or a pharmaceutically acceptable salt thereof, together with at least one pharmaceutically acceptable excipient.

* * * * *